NOVEMBER, 1950

The Review of Gastroenterology

OFFICIAL PUBLICATION

NATIONAL GASTROENTEROLOGICAL ASSOCIATION

Esophageal Dysphagia, Associated with Gallbladder Disease

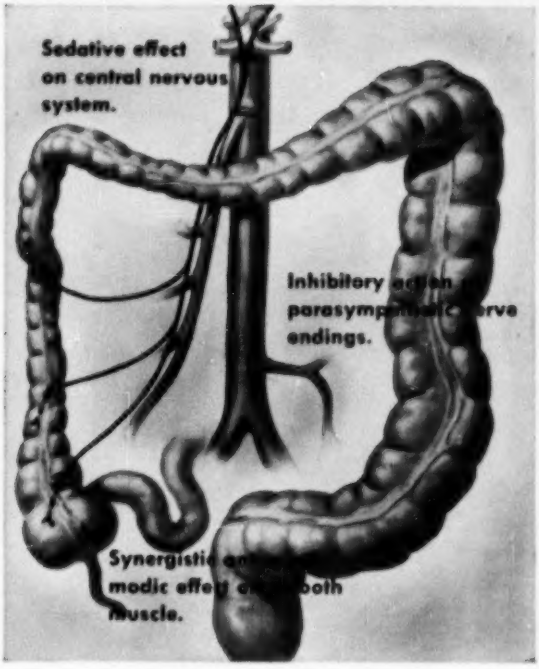
Chronic, Nonicteric Hepatomegaly With Dyspepsia

Tumors of the Esophagus Below the Mucosa

Pancreatic Lesions in Hodgkin's Disease

Hemochromatosis

VOLUME 17 NUMBER 11



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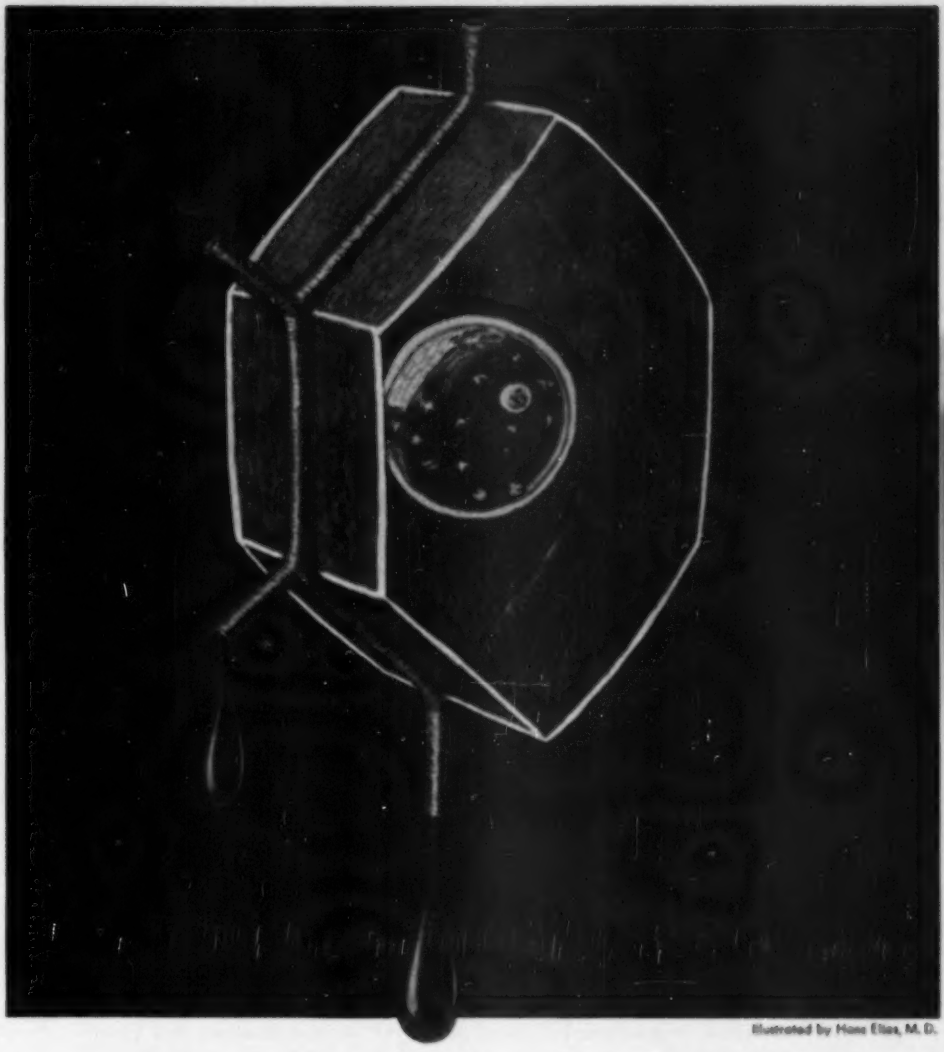

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The REVIEW *of* GASTROENTEROLOGY

(Incorporating the American Journal of Gastroenterology)

The Pioneer Journal of Gastroenterology, Proctology and Allied Subjects in the United States and Canada

Volume 17 NOVEMBER, 1950 Number 11

CONTENTS

	Page
Editorial Board	984
General Information	986
Tumors of the Esophagus Below the Mucosa and Their Roentgenological Differential Diagnosis — *Richard Schatzki, M.D. and L. E. Hawes, M.D.*	991
Chronic, Nonicteric Hepatomegaly With Dyspepsia — *M. B. Handelsman, M.D., I. Richard Schwartz, M.D. and M. Perlmutter, M.D.*	1015
Pancreatic Lesions in Hodgkin's Disease — *Antonio Rottino, M.D. and Charles A. Crown, M.D.*	1033
Mesenteric Thrombosis of Midjejunum with Resection and Recovery — *Jose S. Licha, M.D. and L. M. Rosati, M.D.*	1037
Gastroileostomy Following Subtotal Gastrectomy — *Charles Windwer, M.D., F.A.C.P. and David Farber, M.D., F.A.C.S.*	1040
Esophageal Dysphagia, Associated With Gallbladder Disease — *Maurice Feldman, M.D.*	1044
Hemochromatosis — *Isidore A. Feder, M.D., F.A.C.P., Leo Gitman, M.D. and Julian B. Hoffman, M.D.*	1048
Results of Peptic Ulcer Treatment With Protein Supplements — *Lester M. Morrison, M.D.*	1058
Psychosomatic Proctology — *Alfred J. Cantor, M.D.*	1068
Corticodiencephalic Gastrointestinal Syndromes in Epileptics (Part XI) — *Thomas S. P. Fitch, M.D., F.A.C.S., Albert W. Pigott, M.D., B.S. and Samuel Weingrow, M.D.*	1075
Chapter Activities	1096
News Notes	1097
In Memoriam	1103

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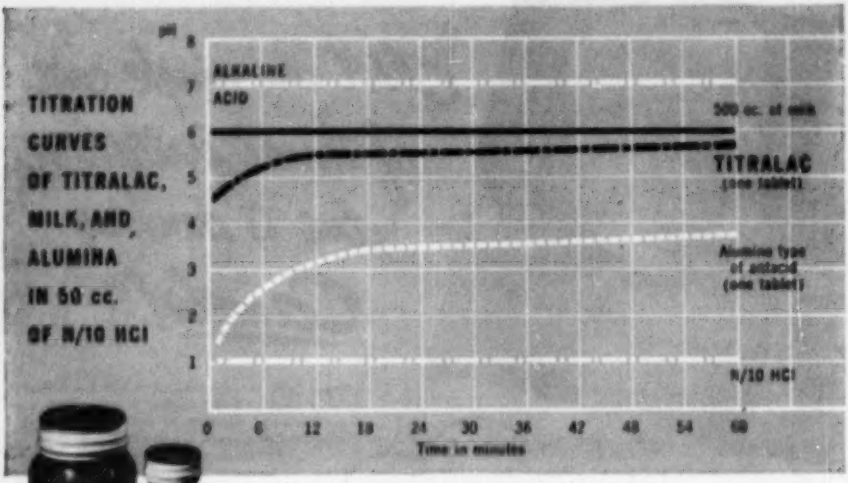

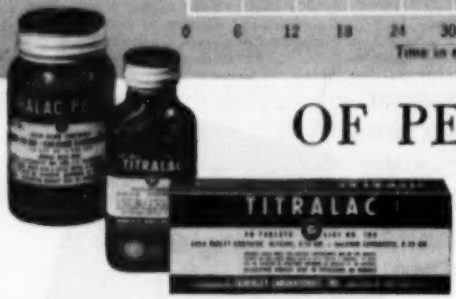

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Volume 17 NOVEMBER, 1950 Number 11

TUMORS OF THE ESOPHAGUS BELOW THE MUCOSA AND THEIR ROENTGENOLOGICAL DIFFERENTIAL DIAGNOSIS*

RICHARD SCHATZKI, M.D.†
and
L. E. HAWES, M.D.†
Boston, Mass.

Lesions of the esophagus which originate outside the mucosa have received scant notice in the earlier roentgenological and clinical literature. Up to 1941 we were able to find only four published cases which belonged to this group and had been examined roentgenologically. At that time the authors published six cases of intramural extramucosal lesions of the esophagus[15]. At the same time an attempt was made at establishing the characteristics of these lesions experimentally. The results of these studies were found to be helpful in the following years. Enough experience has been gathered in the meanwhile by the authors and by others[1-3,5-7,9-11,13,14], to warrant re-evaluation of the problem. The differential diagnosis from other lesions has been of particular significance since the rapid advances of esophageal surgery promotes more active attack on lesions of the esophagus.

The old cases will be briefly reviewed, some of the more recent cases will be described, the basic principles involved will be discussed, and the limitations in the differentiation of the various lesions will be emphasized.

Tumors which originate below the mucosa but become pedunculated during their development will not be included in this discussion.

Of recent articles, the one by Harper[6] and Tescenco[8] is emphasized since it contains a thorough analysis of the roentgenological differential diagnosis.

Review of the Previously Published Cases of Authors

Case 1:—M. W., girl, 19 years old, who had had two years of attacks of dull pain beneath the lower sternum lasting for two or three days, more marked after meals. For the last eight months there had been some dysphagia and she had lost ten pounds in weight.

The roentgenological examination showed a mass closely related to the esophagus at the level of the aortic arch. In the profile view there was a sharp angle

*Read before the Fourteenth Annual Convention of the National Gastroenterological Association, Boston, Mass., 24, 25, 26 October 1949.

†From the Departments of Radiology, Massachusetts General Hospital, Boston, Mass., Mount Auburn Hospital, Cambridge, Mass., Faulkner Hospital, Boston, Mass.

between the normal mucosa and the beginning of the mass, and the face on view showed a sharp edge corresponding to the circumference of the mass.

At operation a neurofibroma arising in the wall of the esophagus was shelled out.

Case 2:—P. S., a woman, 26 years old, had had six months of intermittent attacks of vomiting and regurgitation of bulky foods lasting from one to three days. The sensation of pressure beneath the mid sternum developed gradually.

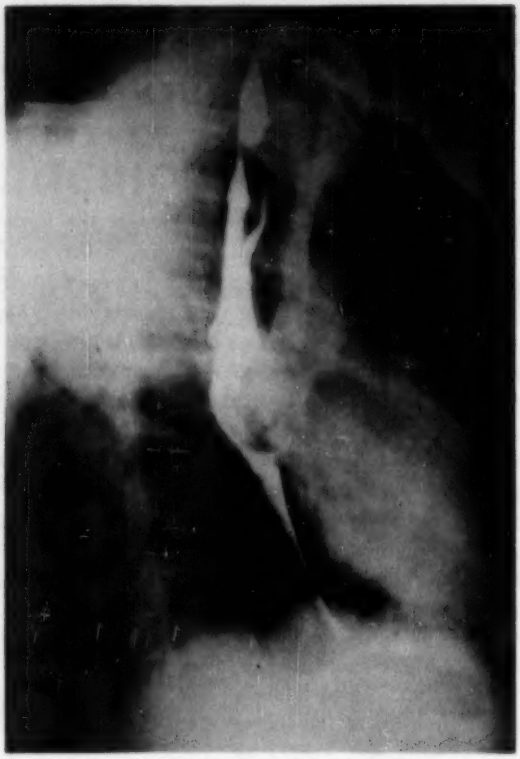

Fig. 1—Case 7. Leiomyoma of the esophagus. Note the sharp edge between the tumor edge and the normal esophagus.

Roentgenologically, a round 3.5 cm. mass was found in close proximity to the esophagus at the junction of middle and distal third producing a similar defect as in Case 1. The mass moved with the esophagus in breathing and swallowing.

An intramural bronchiogenic cyst was removed at operation.

Case 3:—H. L., a man, 43 years old, complained of increasingly severe productive cough and aching sensation beneath the sternum increased by lying on his back. He showed a 10 cm. round mass which displaced the esophagus backwards close to the carina, spreading the carina apart and narrowing the left main bronchus

resulting in collapse of the left lower lobe. The mass moved with the esophagus and showed the same roentgenological characteristics in regard to the esophagus as Case 1.

At operation a cyst was found buried in the muscular layer of the esophagus and attached to the left main bronchus. The origin of the cyst could not be definitely established.

Case 4:—A physician, 35 years old, had had an unusual sensation for a few months beneath the sternum during swallowing not depending on the type of food. His complaints were thought to be functional in nature by previous examiners.

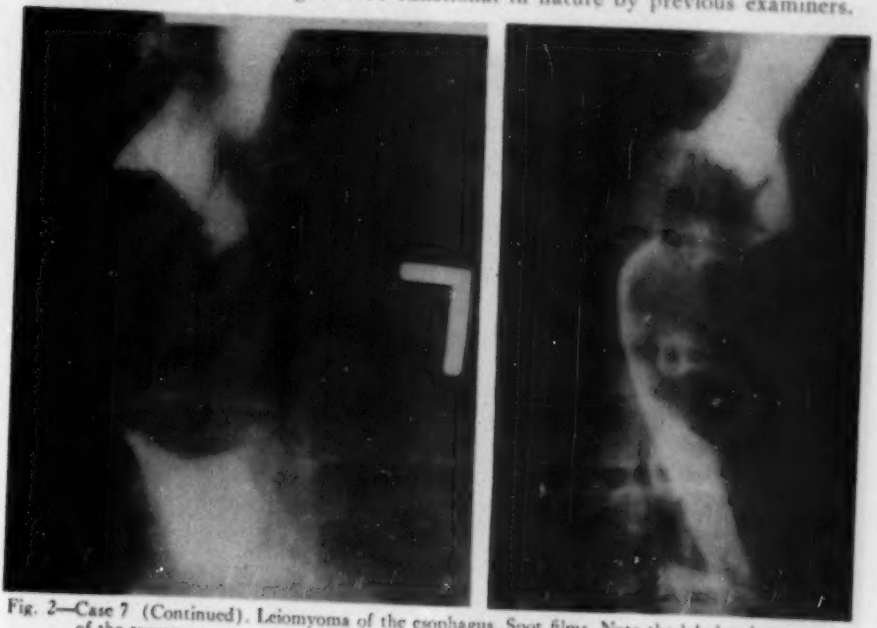

Fig. 2—Case 7 (Continued). Leiomyoma of the esophagus. Spot films. Note the lobulated appearance of the tumor.

Roentgenologically, a small smooth although slightly lobulated filling defect was seen on one wall of the esophagus at the level of the carina. Esophagoscopically, the mass was found to be covered by normal mucosa.

The mass showed only questionable slight increase in size over a period of two years. No operation was performed.

Case 5:—A woman, 36 years old, complained of sour eructation, nausea, and some epigastric pain with a ten pound weight loss in six months. She showed a lobulated mass closely connected to the esophagus at the junction of middle and lower thirds. The mass was seen to bulge into the lumen as well as away from the lumen. It showed the same sharp edges as described in Case 1. Normal mucosal folds were seen, apparently representing the esophagus on the opposite wall.

Esophagoscopically, the mucosa was seen to be intact over the mass. No operation or biopsy was performed.

Case 6:—A man, 53 years old, with indefinite epigastric pain. He showed a small, slightly lobulated, sharply defined filling defect in the lower third of the esophagus.

Esophagoscopically, the mucosa was intact. Attempts at biopsy were unsuccessful. No operation was performed.

New Cases of Authors

Case 7:—A. S., U334,605, M.G.H., a 31-year old male, had for eighteen months a feeling of pressure under the mid sternum greatly increased during meals.

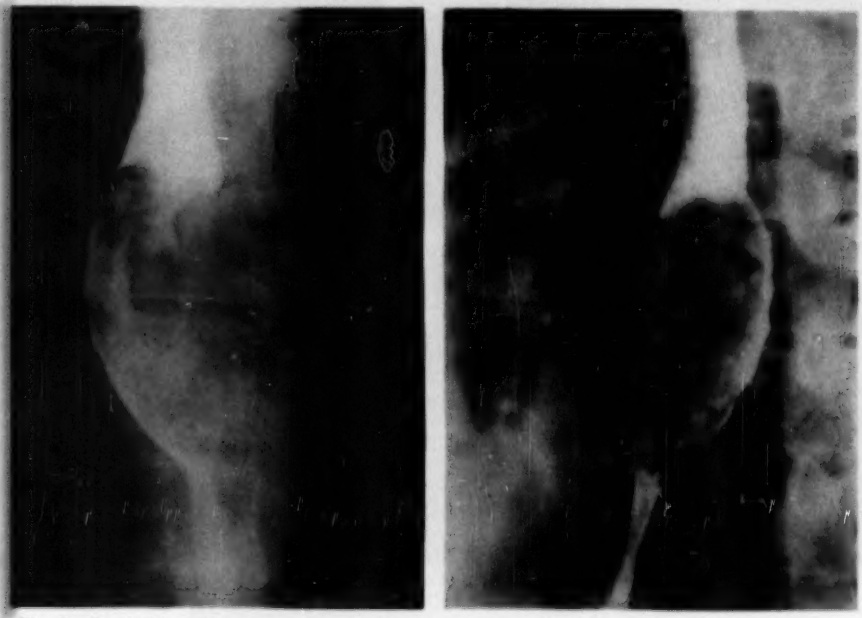

Fig. 3—Case 8. Neurofibroma of the esophagus. Note the granular appearance over the tumor mass on the right hand illustration. This probably does not represent the actual shape of the tumor surface but is a happenstance filling of the thin slit between the tumor and the opposing wall of the esophagus.

Roentgenologically, a lobulated smooth mass with sharp edges was demonstrated in the mid third of the esophagus. It appeared not ulcerated (Figs. 1 and 2). After rapid drinking there was considerable difficulty due to barium which had piled up in the upper esophagus and spilled into the pharynx. If the patient drank slowly he did well.

At operation, (Dr. R. H. Sweet) a lobulated tumor which was wrapped around three-quarters of the circumference of the esophagus was removed without breaking the mucosa.

Histology:—Leiomyoma.

Case 8:—P. W., U582,867, M.G.H. For ten weeks this 40-year old man had had a sensation of food sticking under the mid sternum. At times the food regurgitated. He had lost ten pounds of weight.

Roentgenologically, a smooth ovoid 7 cm. mass was seen in the wall of the esophagus 6 cm. below the arch of the aorta. It caused some delay in the passage of barium (Fig. 3).

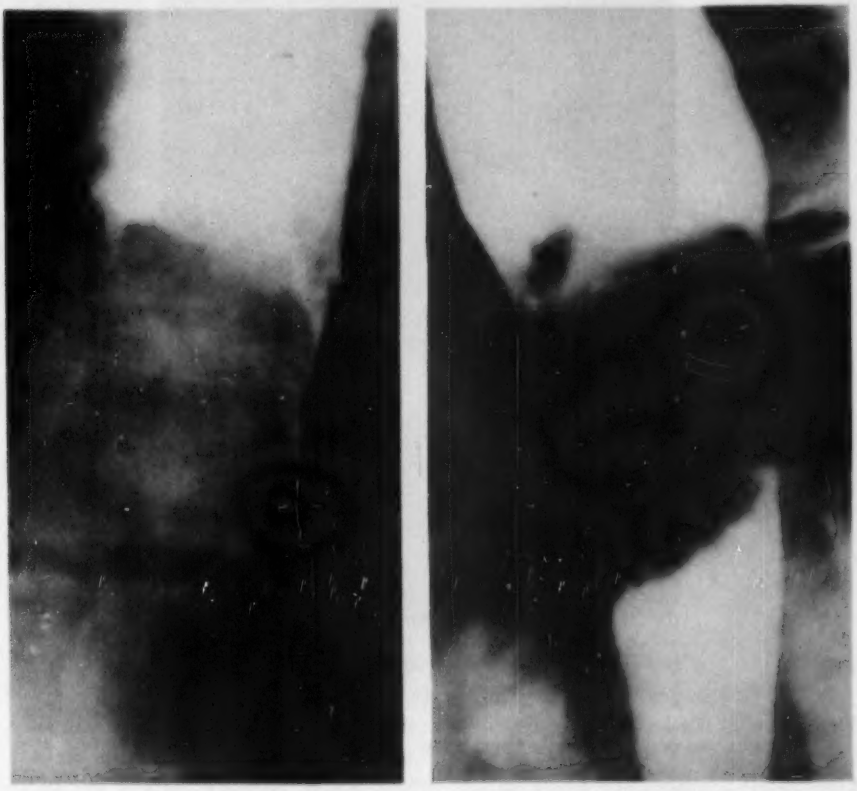

Fig. 4—Case 9. Leiomyoma of the esophagus. The amount of obstruction is unusual for an intramural extramucosal tumor of this size.

The appearance was consistent with an intramural extramucosal tumor of the esophagus, probably benign.

Operation, (Dr. R. H. Sweet) showed a bilobate tumor with a 3 cm. rounded intraluminal portion covered with mucosa, and a slightly larger 4.5 cm. firmer mass bulging out from the wall.

Histology:—Neurofibroma.

Case 9:—R. J. R., U561,289, M.G.H.*. For six months this 49-year old man had had increasing pain under the lower sternum while eating and a sensation of pressure until the food passed into the stomach. The difficulties increased until he was unable to swallow solid food. Twenty-five pounds of weight had been lost.

A 5 cm. oval sharply defined mass was seen in the mid esophagus, attached to its left anterior wall. The mass appeared slightly nodular and not ulcerated (Fig. 4).

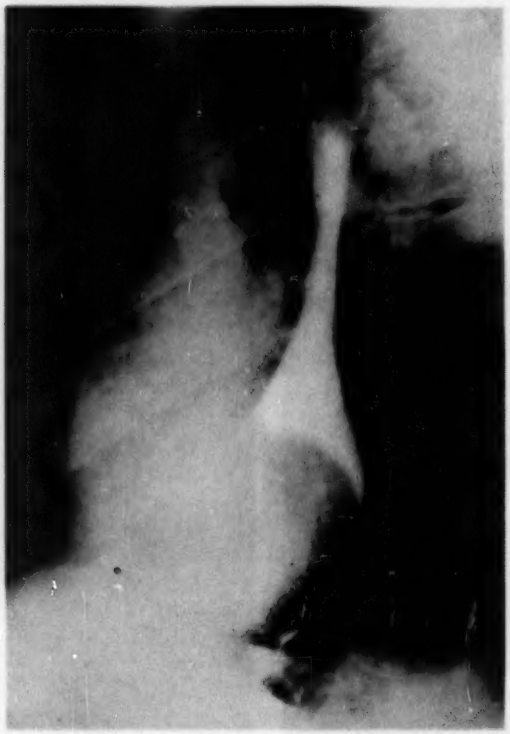

Fig. 5—Case 10. Tracheobronchial cyst of the wall of the esophagus. Note the intimate relationship between the esophagus and the tumor mass.

Only small amounts of barium passed by the lesion. Stomach showed markedly swollen folds and a large duodenal ulcer.

Cancer of the esophagus and active duodenal ulcer were thought to be the most likely diagnosis.

At operation, (Dr. R. H. Sweet) a 4 cm. smooth, slightly lobulated mass was enucleated.

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*Published as case record of the Massachusetts General Hospital, No. 33252. New England J. Med. **236**:955-957, 1947.

Histology:—Leiomyoma.

Remarks:—The diagnosis of polypoid cancer rather than extramucosal tumor was made since no soft tissue mass was seen in this large tumor before the administration of barium. In addition, the marked obstruction was thought to be unusual for an extramucosal lesion. Retrospectively, the absence of ulceration should have been strongly in favor of extramucosal lesion, and this diagnosis should have been made.

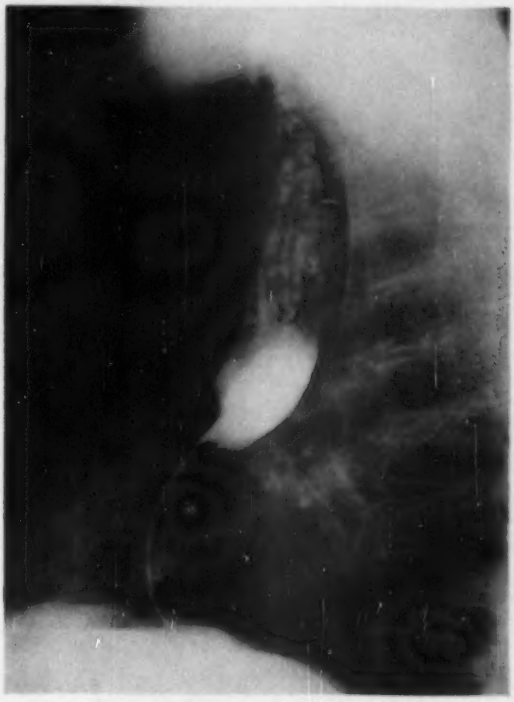

Fig. 6—Case 11. Hematoma of the wall of the esophagus causing the appearance of an intramural extramucosal lesion. (See text for further details.)

Case 10:—M. J. W., U563,620, M.G.H.†, a 43-year old man had for 15 years suffered with substernal pain during meals. For two months, difficulty in swallowing had been present and regurgitation occasionally occurred. Weight loss was 16 pounds.

Roentgenologically, an 8 cm. soft tissue mass was seen between the heart and the spine. It caused the lumen of the esophagus to spread in a semicircular arch (Fig. 5). There was only partial obstruction present.

†Previously published as case record of the Massachusetts General Hospital, No. 33182. New England J. Med. **236**:672-674, 1947.

Findings were those of an intramural extramucosal tumor of the esophagus.

An intramural esophageal cyst was enucleated (Dr. R. H. Sweet).

Histologically it proved to be a cyst of misplaced tracheobronchial epithelium (tracheobronchial cyst of the esophagus wall) (Dr. T. B. Mallory).

Case 11:—A. E. C., U550,283, M.G.H., a 56-year old man with cirrhosis of the liver had repeated injections with sclerosing solutions in esophageal varices. Approximately one month after the last injection he developed mid epigastric boring pain, followed by substernal pain while eating, and by regurgitation of food.

Fig. 7—Case 11 (Continued). Hematoma in the wall of the esophagus causing the appearance of an intramural lesion.

Roentgenologically, a large soft tissue mass was seen in the posterior mediastinum. The mass pressed on the esophagus and caused almost complete obstruction 8 cm. above the diaphragm raising the question of a hematoma in the mediastinum (Figs. 6 and 7).

The patient vomited a large amount of blood in the afternoon following the examination, and died in shock the next morning.

Autopsy showed a hematoma in the lower esophageal wall rupturing into the aorta and into the esophageal lumen.

Remarks:—The sharply defined edge of the lesion suggested an intramural lesion, and the possibility of an intramural hemorrhage was thought of. In lesions of this magnitude the differentiation from extrinsic pressure may be impossible since pressure in a confined space will cause an extrinsic lesion to assume some of the characteristics of an intrinsic lesion.

Discussion of the Roentgenological Features

The described cases have certain roentgenological features in common. They are mainly based on the fact that the lesions are so closely attached to the esopha-

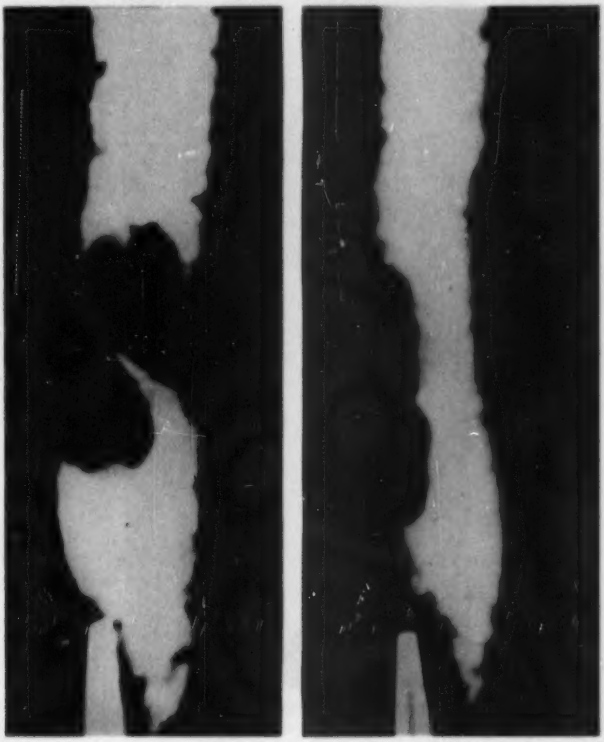

Fig. 8—Artificially produced submucosal tumor (submucosal paraffinoma in a resected piece of jejunum). Note the sharp definition of the lesion which is indistinguishable from a lesion of the mucosa. (*From Schatzki, R. and Hawes, L. E., Am. J. Roentgenol.* **48**:1-15,1942.)

geal wall that the mucosa is stretched over them and closely imitates the surface of an intramural extramucosal lesion. In the profile picture there is a sudden step into the lumen with an abrupt angle wherever the tumor mass starts. In the face on view the edge of the lesion is sharply outlined.

The mucosal pattern overlying the lesion is usually obliterated by stretching, but at times the normal mucosa of the noninvolved wall of the esophagus opposite the lesion may be projected into the defect.

The vast majority of the extramucosal lesions of the esophagus have a smooth, although at times lobulated surface. They are either spherical or ovoid in shape. The soft tissue mass of the lesion is frequently seen fitting closely into the defect of the barium column. Usually about half of this mass seems to lie within, the other half outside the esophagus (Harper).

Motion of the lesion with swallowing indicates close relationship to the esophagus.

Fig. 9—Artificially produced intramural extramucosal tumor of the esophagus. (Inflated rubber balloon within the muscularis of a postmortem esophagus.) Note the sharp edges of the lesion with the esophagus indicating the exact demonstration of the actual shape of the balloon. (*From Schatzki, R. and Hawes, L. E. Am J. Roentgenol. 48:1-15, 1942.*)

It should be emphasized that normally only the larger extramucosal lesions produce any obstruction to the flow of barium, whereas there is none in the smaller ones. The defect produced by the smaller tumors is at times only visible in certain phases of the swallowing act while in other phases the esophagus may appear almost normal.

Review of Previous Experimental Studies

In order to study more basically the roentgenological appearance of lesions in the wall of the esophagus, studies were performed on artificially produced lesions[12]

(Figs. 8-11). All studies were performed on fresh specimens. Submucosal lesions were created by the injection of paraffin into the submucosa. Intramuscular lesions in the wall of the esophagus were produced by inflating a small rubber balloon which had been inserted in the muscular layer of the esophagus. Extrinsic lesions were studied by pressing a piece of cork against the esophagus. Finally a piece of

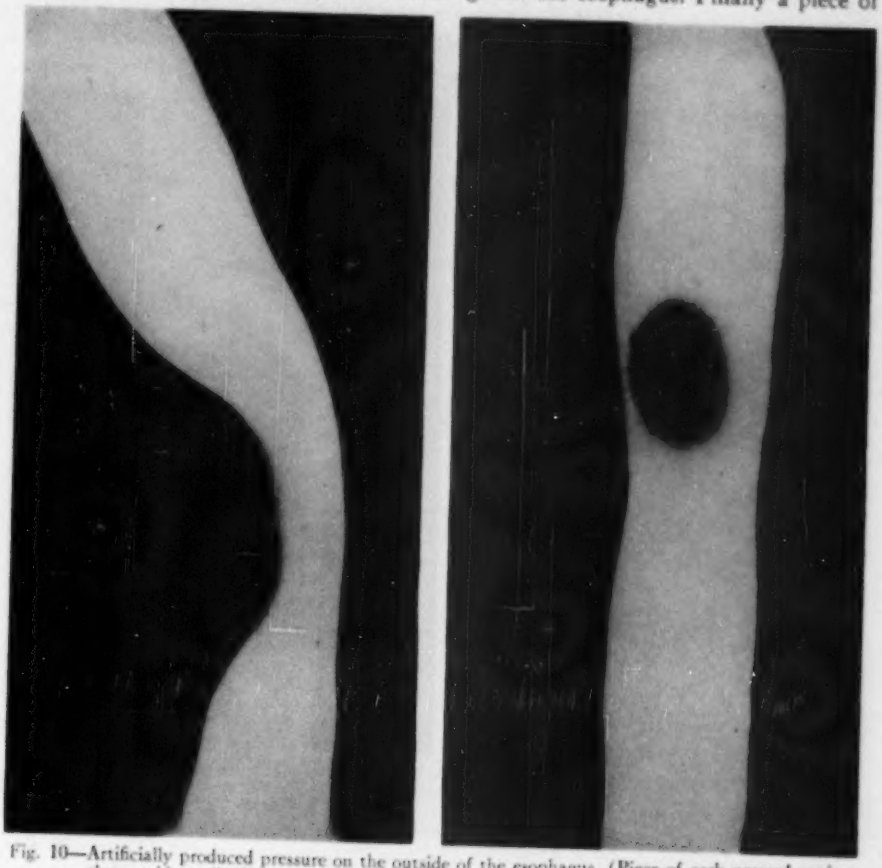

Fig. 10—Artificially produced pressure on the outside of the esophagus. (Piece of cork pressed against the outside wall of a postmortem esophagus.) Note the gradual slope in the region of the pressure in profile and face on views in contradistinction to the sharp edge of the intramural lesion. (*From Schatzki, R. and Hawes, L. E. Am. J. Roentgenol.* **48**:*1-15, 1942.*)

cork was sewed onto the outside of the esophagus to imitate an extrinsic lesion which had become attached to the esophagus.

These studies showed that a lesion in the submucosa or in the wall of the esophagus below the submucosa was indistinguishable from a lesion in the mucosa itself. The radiological picture showed the exact shape of the lesion both in profile and face on view. In other words, the thin layer of the overlying esophageal wall

was not sufficient to obliterate the exact shape of the mass, and the lesion in this respect did not look in any way different from a lesion of the mucosa itself. The same applied to an extrinsic lesion which had been rigidly attached to the esophagus. On the other hand, a lesion which just pressed against the esophagus and was not attached showed a definite difference. The edges of the pressure defect were hazy in the face on view and in the profile view there was a gradual rather than a sudden change between normal and abnormal areas. The size of the defect varied with the degree of pressure. The extrinsic lesion which was attached only on one

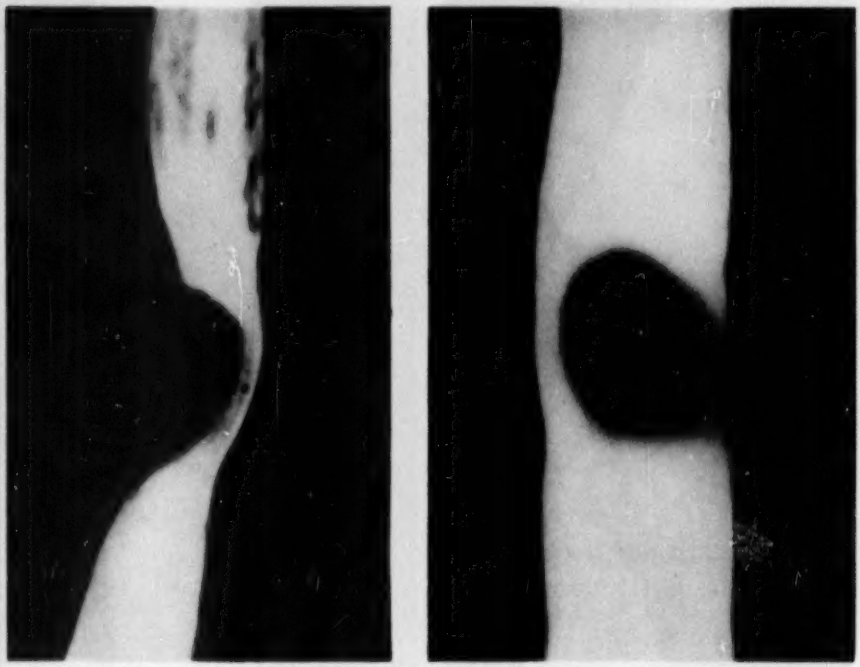

Fig. 11—Artificially produced extrinsic tumor which is attached to the esophageal wall in its upper pole. (A piece of cork pressed against the esophageal wall and sewed onto it with its upper pole.) Note the sharp upper edge of the lesion in profile and face on view compared with the unattached gradually sloping lower edge in both views. (*From Schatzki, R. and Hawes, L. E. Am. J. Roentgenol.* **48**:1-15, 1942.)

pole but not on the other pole showed the characteristics of an unattached extrinsic lesion on one pole and the characteristics of an intrinsic lesion on the other pole.

Differentiation of Intramural from Extrinsic Lesions

The main difficulty and clinically most important differential diagnostic problem is the decision as to whether or not a lesion arises outside the esophagus or within its wall. The recognition of the extrinsic character of the lesion is at times easy either by the fact that it shows the characteristics described above for an extrinsic lesion or by the fact that it can be clearly recognized as a part of a struc-

ture which lies outside the esophagus, e.g., aorta, bronchus, etc. In other instances the decision is quite difficult. A few examples will illustrate the problems involved.

Case 12:—Mrs. P. This patient was sent to the x-ray department because a lesion at the junction of middle and distal third of the esophagus had been suspected to be cancer in another hospital. The roentgenological examination clearly indicated the extrinsic character of the lesion with gradual sloping of the edges of the defect

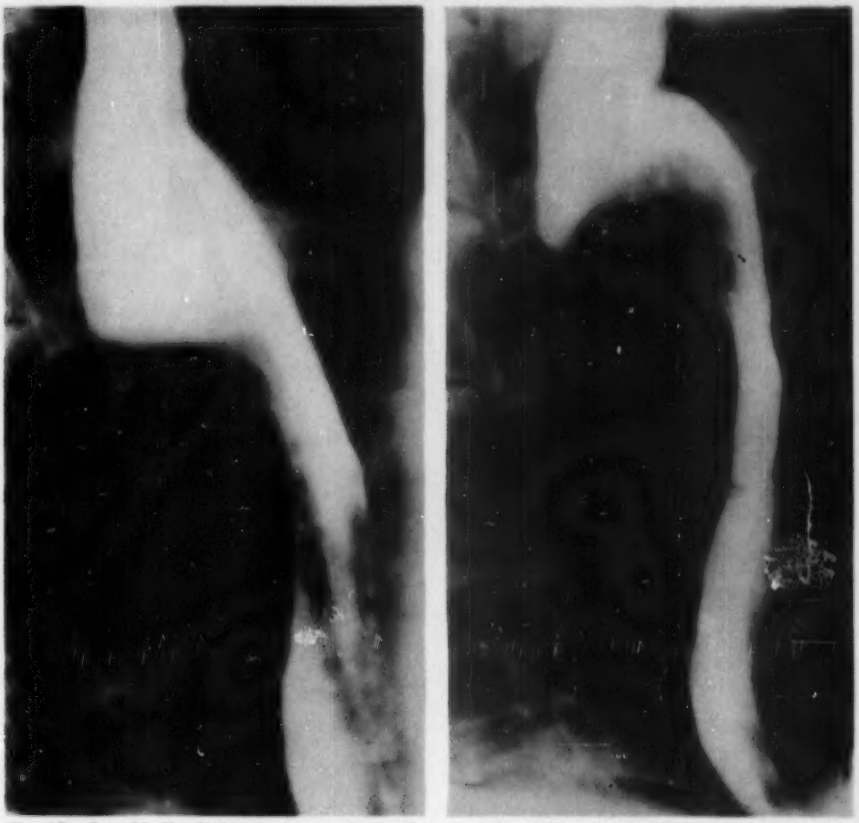

Fig. 12—Case 12. Extrinsic pressure on the esophagus produced by an unusually tortuous descending aorta.

(Fig. 12). The structure of an abnormally tortuous aorta which crossed over to the right side in its descending portion could be outlined as cause of the pressure.

Case 13:—S. S. F., U496,940, M.G.H.* A woman, 43 years old, entered the hospital with a 6 weeks' story of dysphagia. While eating, she was suddenly seized by a severe epigastric pain that radiated to the axillary border and the angle of the

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right scapula. The pain gradually disappeared after eating was completed. Thereafter, any attempt to eat solid foods precipitated another attack. Lately, even soft food and hot or cold drinks brought on a reaction.

Roentgenological examination at Union Hospital, Framingham (Dr. Joseph Ferrucci) revealed a sharply defined defect in the mid portion of the esophagus (Fig. 13). It had all the characteristics of an intramural extramucosal lesion.

At operation a group of tuberculous nodes was found in this region attached to the esophagus.

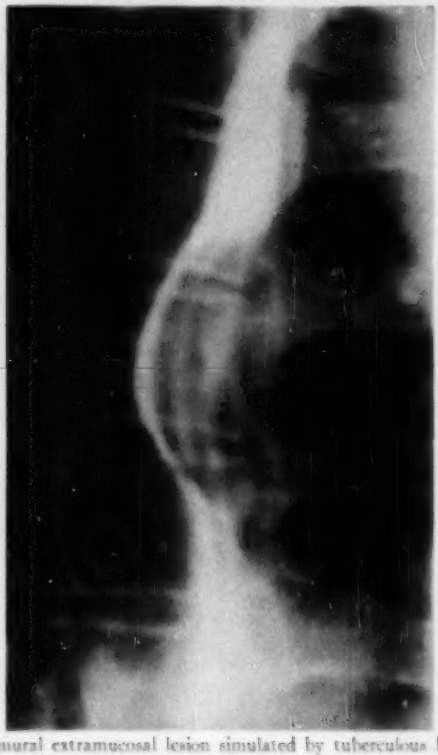

Fig. 13—Case 13. Intramural extramucosal lesion simulated by tuberculous lymph node which is attached to the esophagus. The surface of the lesion corresponds exactly to the shape of the lymph node and from its radiological appearance the lesion is indistinguishable from an intramural extramucosal lesion. (For further details see text.)

Remarks:—An extrinsic lesion attached to the esophagus had produced the characteristic appearance of an intramural lesion of the esophagus.

Case 14:—Dr. B.F.F., (M.A.H.), a physician, 40 years old, had pain between the scapulae at the level of the 7th and 8th thoracic vertebrae brought on by deep inspiration or expiration, with intermittent fever with temperature between 99 and 100 degrees. Pain was associated with dysphagia. Laboratory findings were negative except for slight leucocytosis.

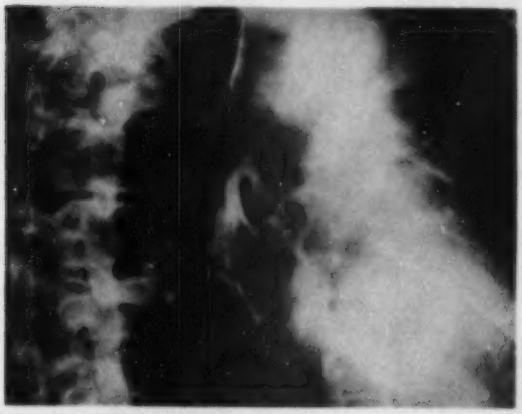

Fig. 14—Case 14. Intramural lesion simulated by lymph node which is attached to the wall of the esophagus. See also Figs. 15-17. (See text for further details.)

Radiological examination showed a small sharply defined defect in the esophagus (Dr. William Butler, Providence, R. I.). In profile the edge of the defect

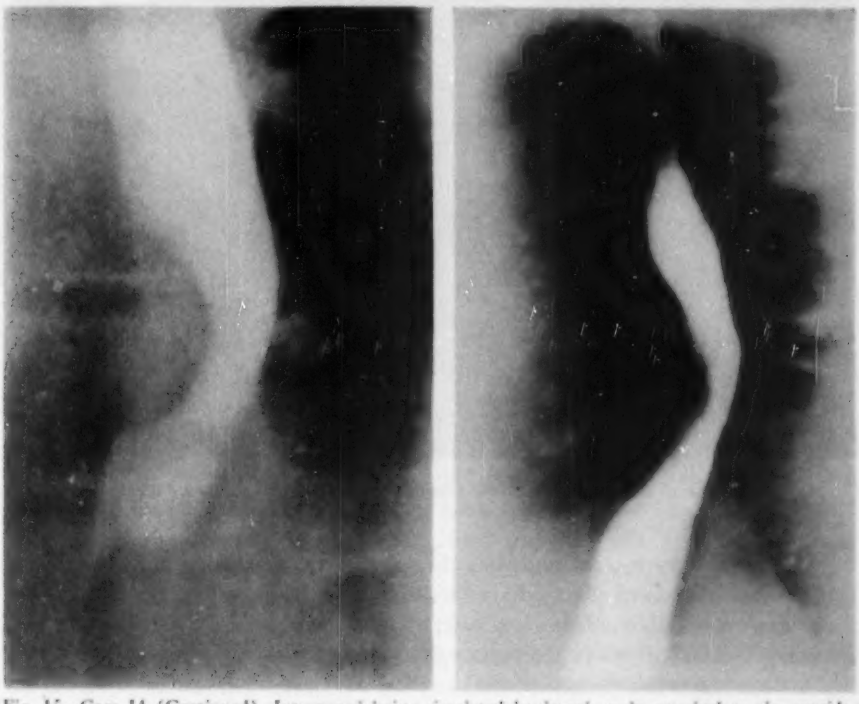

Fig. 15—Case 14 (Continued). Intramural lesion simulated by lymph node attached to the outside wall of the esophagus.

formed abrupt steps against the wall of the esophagus (Figs. 14 and 15). Examination eight days later showed the defect slightly less marked. Now, only its lower edge formed a sharp step with the esophageal wall (Fig. 16). The symptoms improved one week after this x-ray examination. He was seen by a chest surgeon, and the question of operation was discussed with the considerably disturbed patient. There were enough unusual features present to warrant some delay. Examination three weeks later showed the lesion to have disappeared (Fig. 17). All the symptoms had gone.

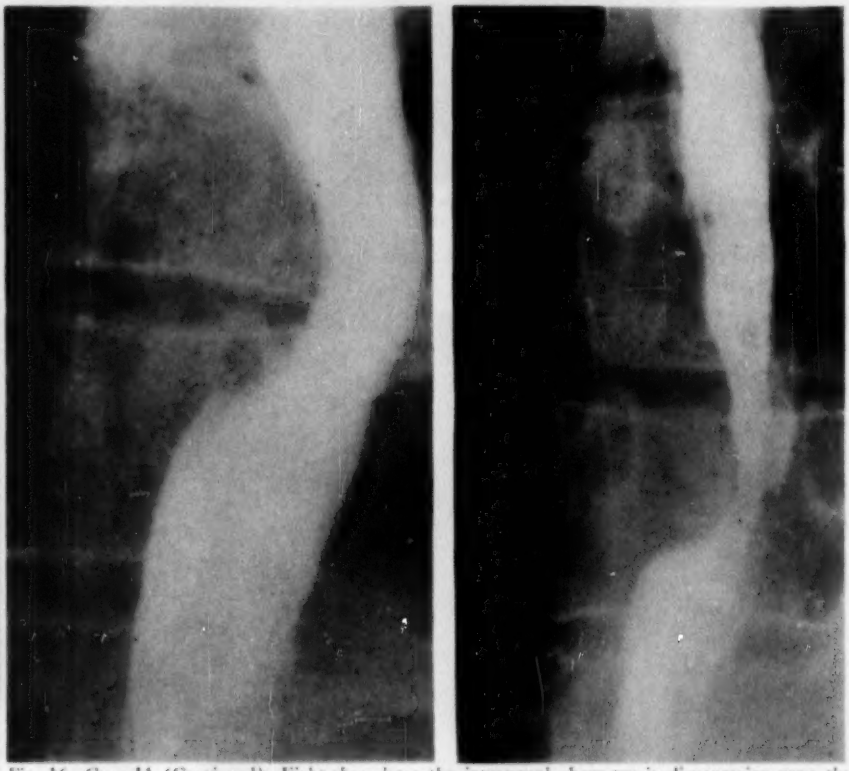

Fig. 16—Case 14 (Continued). Eight days later the intramural character is disappearing near the upper edge of the lesion. The lesion appears now very similar to the experimental study in Fig. 11, i.e., a lesion which is attached at one pole, in this case the lower pole, and not attached at the upper pole.

Approximately two months after the onset of the original symptoms, patient had another episode of illness characterized by low grade fever, nasopharyngitis, pain between shoulder blades but without dysphagia. The esophagus showed a questionable small defect in the previously described area. On being given streptomycin his temperature became normal in a few days and all symptoms disappeared completely.

Remarks:—An extrinsic lesion, probably an enlarged lymph node, had become partially attached to the esophagus and caused a defect similar to that of an intrinsic lesion. It is noteworthy to see how this lesion imitated the character of an intrinsic lesion on one edge whereas the other edge had more the appearance of an unattached extrinsic lesion. It is possible that this lesion was attached to the esophagus only on one pole (Compare Fig. 16 with Fig. 11).

Fig. 17—Case 14 (Continued). Three weeks later the pressure defect has completely disappeared. (See text for further details.)

Not infrequently the left main bronchus causes a slight pressure defect on the esophagus. At times, and particularly in elderly individuals, this defect becomes quite marked and sharply defined, having the appearance of an extrinsic, attached lesion (Fig. 18). It appears likely that in these cases the left main bronchus is adherent to the esophagus by adhesions. This fact may become of some diagnostic significance. If, in the presence of mediastinal pathology of unknown origin in a young person the left main bronchus produces the defect of an

extrinsic lesion attached to the esophagus, the assumption can be made that the process has caused adherence between the esophagus and the left main bronchus. At that age, inflammatory lesions are most apt to produce such adhesions and inflammation rather than tumor is the likely diagnosis. This sign is less valuable in elderly persons, since the sharply defined defect of the esophagus where it crosses the left main bronchus is not infrequently found in apparently healthy people above the age of 60 years.

Fig. 18—Sharply defined pressure defect of the esophagus where the left main bronchus crosses over it. This probably indicates adhesion of the esophagus to the bronchus.

Differentiation of Extramucosal from Mucosal Lesions

The experimental studies showed that the basic features of intramural extramucosal lesions are the same as those of lesions of the mucosa. In each instance the barium demonstrated the exact shape and extent of the lesion as far as the wall was concerned in the tangential view as well as in the face on view. The differentiation between lesions of the mucosa and extramucosal intramural lesions is therefore not based on a definite roentgenological principle but rather on differences in the anatomical appearance: Lesions arising from the mucosa are usually ulcerated. Lesions arising below the mucosa are usually not ulcerated. The mucosal lesions are usually more irregular than the extramucosal lesions. The normal

mucosa of the opposite wall is more apt to show in extramucosal lesions. Extramucosal lesions frequently can be seen to produce a large soft tissue mass. This is much less common in lesions arising from the mucosa and particularly rare in polypoid lesions of the mucosa, the only ones which otherwise may offer differential diagnostic difficulties.

Malignant tumors which start in the wall below the mucosa and then protrude secondarily in the lumen can usually not be differentiated from primary lesions of the mucosa particularly when they have become ulcerated. They are quite commonly larger than the average carcinoma.

The differentiation of very small mucosal lesions from intramural lesions may be extremely difficult or impossible.

Fig. 19—Case 15. Small cancer of the lower end of the esophagus increasing rapidly in size within three months. See similarity of this small cancer with the small intramural extramucosal tumor in previous publication[15].

Case 15:—(Courtesy of Dr. Alice Ettinger, New England Medical Center). A patient with uncharacteristic dyspeptic symptoms showed a small tumor in the lower end of the esophagus (Fig. 19a). Three months later he had dysphagia and intense retrosternal pain. The tumor had grown (Fig. 19b).

Note the similarity of this cancer at its first examination with the extramucosal lesion in Case 6, of our previous publication[15]. The finely irregular surface of the tumor is the only difference.

Since basically the mucosal lesion has the same characteristics as the extramucosal intramural lesion none of the criteria by itself is pathognomonic for the origin of the tumor. It is the combination of the various factors which allows the differentiation of the lesions in most instances. We agree however, with Lowman,

Shapiro, and Kushlan[12] that the differentiation at times is impossible. These authors describe three cases of gastric cancer which closely simulated the appearance of intramural extramucosal lesions. They stress the presence of fine reticulation over the surface of two of these lesions, and postulate that this may be a sign of malignancy of the tumor regardless of whether it arises in the mucosa or submucosa. We believe that such reticulation, if constant and not produced by happenstance settling of barium over the surface of the lesion, is greatly in favor of intramucosal origin of the lesion for the reason that these lesions are more irregular than the intramucosal lesions. We doubt, however, that this reticulation will enable one to make a differential diagnosis between benign and malignant intramural extramucosal lesions.

Summary

Intramural extramucosal lesions of the esophagus are described. They include neurofibromas, leiomyomas, bronchiogenic cysts, and a case of hematoma in the wall of the esophagus.

The salient roentgenological features of these lesions are analyzed.

Experimental studies are reviewed which attempt to differentiate intramural from extrinsic and mucosal lesions.

It is usually easy to differentiate lesions which are extrinsic to the esophagus and not attached from those which either arise in the wall of the esophagus or have become secondarily attached to the esophagus.

The differentiation of mucosal lesions and extramucosal lesions of the esophagus as well as of the extrinsic lesions which have become attached to the esophagus is considerably more difficult. It is primarily based on the anatomical characteristics of the lesions. The differentiation, particularly of very small or very large lesions, may be impossible.

References

1. Adams, H. D.: Primary Tumors of the Esophagus. S. Clin. North America. **27**:587-591, 1947.
2. Adams, R.: Fibroma of Esophagus. Lahey Clin. Bull. **3**:72-81, 1943.
3. Brock, R. C.: Cardioesophageal Resection for Tumor of the Cardia. Brit. J. Surg. **30**:146-150, 1944.
4. Buckstein, J.: Digestive Tract in Roentgenology. 1948, J. B. Lippincott (p. 64).
5. Calmenson, M. and Clagett, O. T.: Surgical Removal of Leiomyomas of the Esophagus. Am. J. Surg. **72**:745-747, 1946.
6. Harper, R. A. K. and Tescenco, E.: Benign Tumor of the Esophagus and its Differential Diagnosis. Brit. J. Radiol. **18**:99-107, 1945.
7. Harrington, S. W.: Surgical Treatment of Benign and Secondarily Malignant Tumors of the Esophagus. Arch. Surg. **58**:646-661, 1949.
8. Hawes, L. E.: Roentgenological Changes in the Esophagus in Tuberculous Mediastinitis. Am. J. Roentgenol. **51**:575-584, 1944.
9. Hurwitz, A.: Leiomyoma of the Esophagus. Surgery. **25**:304-306, 1949.
10. Kenworthy, R. A. and Welch, C. S.: Leiomyoma of the Esophagus and Cardia of the Stomach. Surgery. **23**:745-752, 1948.
11. Kornblum, K. and Bradshaw, H. H.: Intrathoracic Neurogenic Tumors. Radiology. **37**:391-406, 1941.
12. Lowman, R. M., Shapiro, R. and Kushlan, S. D.: Extramucosal Tumors Simulated by Gastric Carcinoma. Am. J. Roentgenol. **57**:726-735, 1947.
13. Moersch, H. J. and Harrington, S. W.: Benign Tumors of the Esophagus. Ann. Otol., Rhin. & Laryng. **53**:800-817, 1944.
14. Schafer, P. W. and Kittle, C. F.: Esophageal Leiomyoma. J.A.M.A. **133**:1202-1205, 1947.
15. Schatzki, R. and Hawes, L. E.: The Roentgenological Appearance of Extramucosal Tumors of the Esophagus. Am. J. Roentgenol. **48**:1-15, 1942.

Discussion

Dr. Frank J. Borrelli (New York, N. Y.):—I have heard Dr. Schatzki before, perhaps six or seven years ago, in Cincinnati, and I must say that I enjoyed the paper just as much this time. I think that Dr. Schatzki is to be highly complimented. He is modest in his statement that these tumors are being picked up more and more now because of the interest, and because of the surgery. It may be because Dr. Schatzki has brought them to our attention; at least, I can say that for myself. Only since Dr. Schatzki's very interesting paper of several years ago did we go back home and make the men in the department carefully analyze the lesions that they suspected in the esophagus, with an attempt at trying to evaluate them from the same angle that Dr. Schatzki did for us today.

Instead of being simply satisfied with neoplasia of the esophagus, we want to know a little more, and certainly every surgeon would like to know whether the lesion is benign or malignant, whether it is extramucosal, intrinsic, or extrinsic, as Dr. Schatzki has presented it so well for us today.

I am sorry that most of you probably were unable to see Dr. Schatzki's demonstration of some of the earlier slides that he had here, due to the fact that the marker wasn't functioning well, but if you get a chance to hear him again, you should listen to him because the roentgenologic features that he brings out are interesting, important, and very helpful.

He was perhaps a bit hesitant, in speaking to a group of members of the National Gastroenterological Association, in bringing out the point of fluoroscopy, but I think he did mention it, and then passed by it. I don't think it is too elementary to say to this group: "Go back and carefully fluoroscope your patients." I am sure that Dr. Schatzki doesn't go into his fluoroscopic room one or two minutes after he has examined a patient, and expect to see all that he has demonstrated today. It is only after half an hour or forty minutes of good accommodation that you can see these things; otherwise you will be satisfied with just noting a lesion either in the mediastinum or esophagus without further differentiation.

There is one thing, Dr. Schatzki, that I noticed in these slides and in your article, perhaps as a point in differential, that you did not mention, though I am sure you are aware of it. In benign lesions there seems to be filling of barium above and below the lesion, in spite of the fact that the lesion appears large enough to obstruct the esophagus completely, while in the two cases of malignancy you noticed there was very little barium below the lesion.

Again, I think that Dr. Schatzki brings out a very important correlation between the gastroenterologist who must know his symptoms and clinical picture and recognize the symptoms of dysphagia and substernal pressure, and the gastroscopist who must be careful in giving the roentgenologist some facts that are the only features that would help differentiate some of these lesions. As he has told us, many of these lesions are extrinsic, although extensions into the esophagus give an edematous appearance of intramucosal involvement. By careful study and addi-

tional information from the gastroscopist, one can tell something about the mucosa, and be able to further analyze the case.

It is also important, perhaps, to repeat the fact that in the benign lesions ulceration was not noted; however, I think gastroenterologists must remember—and I think Dr. Schatzki did mention it in one of his former papers—that even though ulceration is not present, bleeding might be present; athough these benign lesions do not often cause bleeding.

I want especially to thank Dr. Schatzki, and I think the Association is fortunate in having Dr. Schatzki give us this interesting and very important paper.

Dr. Franz J. Lust (New York, N. Y.):—I agree with Dr. Schatzki that there are quite a number of nonobstructing lesions of the esophagus which are not recognized during the routine gastrointestinal x-ray examination; therefore, I should like to take this opportunity to make a suggestion for the further work.

We have made it routine now to take one of our oblique films of the stomach, taken in the prone position, just after some barium is swallowed.

We then see the esophagus and the stomach on the same 10x12 film, and have a record of the lower part of the esophagus for further reference. If everyone would take a right oblique film in every gastrointestinal series, we would have an additional record without extra expense.

As to the question of the intramural, extramucosal lesion, we had the opportunity to see a patient who had the following history: In 1945 he had a swelling of the glands of the neck. He was not examined by me at that time and his surgeon, Dr. Mettenleiter, found that he had a reticulum cell lymphosarcoma.

The patient was treated by radiation and improved so that he was perfectly well up to about the middle of 1948. At that time, all of a sudden, within a few weeks, he had difficulty in swallowing, and an x-ray examination of his esophagus was performed. There was a narrowing of the esophagus, funnel-shape—no tumor.

There was no loss of weight, no bleeding. There arose the question of diagnosis. We had the patient esophagoscoped, and on two occasions a biopsy was taken and on both occasions the report came back as negative.

We were pondering at that time what kind of lesion we were seeing on all our films, and we decided that probably it was one of those lymphatic tumors due to the long spread of the lesion of the esophagus, and radiation therapy was inaugurated, again with good success for about five months and then there was a close-up again. A tumor was found in the mediastinum.

The patient died about six months after this and a leiomyoblastoma of the esophagus was found. It looked at first as if we had an ulcerating lesion in the middle of the esophagus, but repeated esophagoscopy showed a perfectly normal esophagus, no erosions, no bleeding.

This case emphasizes the difficulty in diagnosis of such cases in spite of roentgenological findings, and in spite of esophagoscopy and biopsy. Only an experienced man like Dr. Schatzki would have been able to make a diagnosis on the first point.

I want to thank Dr. Schatzki again for his excellent presentation.

Dr. Louis L. Perkel (Jersey City, N. J.):—I wonder how many of you feel, as I do, that discussions are usually not unlike supernumerary appendages. Rarely do they add much to the paper. If the discusser agrees with the speaker, he "flowers" him with such expressions as "monumental contribution", and "succinct presentation". If he disagrees, he will attempt to present his own paper and try to compress it into five minutes, when it should take an hour.

Nevertheless, Dr. Schatzki's paper is valuable to us as gastroenterologists. In his paper, which may well be read and re-read by all of us with profit, he has described a syndrome of roentgen signs characteristic of extramucosal, intramural tumors of the esophagus. His work will be of great help in differentiating the various types of esophageal neoplasms.

At this time I wish to make a plea to the younger men not to rely implicitly on their newly purchased and little understood x-ray equipment. They must be taught that x-ray diagnosis is not a substitute or short cut for complete clinical study of a case. There are many pitfalls and errors in diagnosis from x-ray examination alone.

When even an experienced roentgenologist as Dr. Schatzki, who has devoted many years to his specialty, occasionally encounters difficulty in diagnosis, how can one expect the young, inexperienced general practitioner to accurately diagnose lesions of the esophagus or, in fact, any part of the gastrointestinal tract?

I feel that the term "roentgen findings" should be used instead of "roentgen diagnosis". The highest percentage of accuracy in diagnosis can be reached only through clinical studies supplemented and corroborated by roentgen findings and other laboratory studies. In our clinic we instruct our house staff and assistants never to order x-ray examinations before a complete clinical study is made.

Now, one or two points about the paper: I note that Dr. Schatzki claims substernal pain was a most important symptom. In our experience in malignancy, dysphagia was usually the chief and only symptom while substernal pain frequently was secondary or late. In extrinsic lesions, lower substernal pain was more prominent than dysphagia, which was found in his studies also.

Finally, it would be of benefit to the general practitioner to realize that there is no short-cut method in diagnosing gastrointestinal lesions; that the glib talk of the x-ray apparatus salesmen should be regarded skeptically. It would be better for the patient as well as for the reputation of the profession that the young physician heed the advice of experienced men like Dr. Schatzki and judiciously use roentgen findings to corroborate his clinical findings.

Dr. Hyman I. Goldstein (Camden, N. J.):—Dr. Schatzki gave us an excellent paper as one would expect, from an experienced radiologist like the doctor. I was much interested in the report of a case of primary rhabdomyosarcoma of the esophagus. Also, the report of a case of primary reticulum cell lymphosarcoma and one of a primary lymphoblastoma-type of tumor of the esophagus, as just made by Doctor Lust, of New York, also interests me. Sarcoma of the esophagus is rare.

Nearly 30 years ago, I reviewed the literature and published papers on "sarcoma of the gastrointestinal tract", "sarcoma of the liver", "sarcoma of the appendix", and "sarcoma of the tongue and of the esophagus". At that time, I believe, there were only about fifty instances of sarcoma of the esophagus recorded in the literature of the world—and some of these cases were not proved instances of primary tumors.

Why is it that malignant mucosal tumors of the esophagus are so common, while sarcomatous tumors as well as other tissue-type tumors are so rare in the esophagus?

Dr. Richard Schatzki (Boston, Mass.):—I wish to thank the discussers, who certainly did not follow the law which Dr. Perkel tried to lay down and then didn't follow himself.

In regard to bleeding and intramural, extramucosal tumors of the esophagus, bleeding is common with these lesions when they arise in the stomach, or in the small bowel.

The benign submucosal tumors of the esophagus, bleed extremely rarely. I think of all the tumors which we have seen, there was in only one case a slight degree of hematemesis, and that could be easily explained on the basis of vomiting and retching.

The cause for the difference is quite easy to understand. The lesions of the stomach and the small bowel ulcerate because they are digested by the stomach and intestinal juice, and particularly may be digested in the upper small bowel, where the greatest protein digestion takes place.

I did not want to create the impression that retrosternal pain was the most common symptom in these lesions, but I have been impressed by its marked frequency. It often preceded dysphagia, and I think in any patient who has retrosternal pain, it is well worthwhile to investigate the esophagus very carefully.

In regard to the rarity of the sarcomata of the esophagus, I don't know how many we have seen. I think I remember, offhand, four of them. Of course, I have not the slightest idea why they are so much rarer than lesions of the mucosa. I think when you go through the anatomy of the human body, you will find that, in general, tumors of the epidermis and the entoderm are much more common than tumors of the mesoderm.

CHRONIC, NONICTERIC HEPATOMEGALY WITH DYSPEPSIA

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and
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Clinical investigations, stimulated by the large amount of hepatic disease seen during the recent war have demonstrated that acute infectious hepatitis with (or without) jaundice can enter a chronic nonicteric phase. Detection of this later stage clinically depends on (1) the presence of symptoms generally attributed to hepatic dysfunction, (2) the presence of an enlarged or tender liver on examination, (3) a preceding history of jaundice or other illness known to affect liver function, and (4) laboratory evidence of liver damage (including liver biopsies). When all these factors are present there is little difficulty in making an accurate diagnosis of chronic hepatitis in a particular case. However, when one of the above criteria is absent, it is extremely difficult to be certain of the diagnosis, and conclusions drawn from such cases may be inaccurate.

The authors, who had the opportunity during the last war both in Africa and Italy to observe hundreds of soldiers diagnosed as having chronic nonicteric hepatitis, found that in the absence of any reliable test to identify the causative agents of acute infectious hepatitis with jaundice, it was impossible to be certain that most of the so-called "chronic" cases were later stages of a hepatic virus disease merely on the basis of symptoms and the finding of a hepatomegaly. It was gratifying to find after the war that solutions for this problem were proposed by two schools of thought without conclusive evidence for either side. To these two explanations we would like to add a third and much older concept. Before discussing these three viewpoints a brief definition of this clinical syndrome is given.

The symptomatology was fairly similar in most cases. Usually there was a history of easy fatigability, weakness coming after mild exertion, a passive sort of mental lethargy, lack of ambition, and blunting of volitional drives. Practically all of these patients complained of poor appetite, became bloated after meals and belched a great deal. The ingestion of fatty meals was followed by considerable heartburn and frequent regurgitation of food. On physical examination, a liver edge that was sharp, firm and regular, could easily be felt below the costal margin. The liver tenderness varied considerably from patient to patient. In only a few of these patients was a palpably firm splenic edge noted. It should again be emphasized that this clinical picture appeared at a time when the patient had recovered from any acute illness that had been present.

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Etiologies Proposed for This Syndrome

1. *Chronic Hepatitis:*—During World War II, acute hepatitis was one of the most common infectious diseases. Large numbers of cases were seen among American troops after injections of yellow fever vaccine contaminated with an icterogenic virus and almost simultaneously, homologous serum jaundice was recognized. Later, epidemic infectious hepatitis became common in all combat theatres. In the Mediterranean Theatre of Operations alone there were 37,000 cases of acute hepatitis reported among American troops. It was in this area that Barker, Capps, et al.[1], found that ten per cent of their patients with acute hepatitis did not fully recover but continued to manifest "hepatic" symptoms with a persistent hepatomegaly. These workers called such cases "chronic infectious hepatitis without jaundice" and have described active and also inactive forms of this disease. Another large series was seen by Rappaport and Klatskin[2] who collected many cases with relapses and recurrences coming at various intervals, some as long as 27 years after an attack of infectious hepatitis.

Conclusive evidence that chronic hepatitis may follow infectious hepatitis has been presented by Neefe[3], who was able to follow four such cases from the acute stage in volunteers, experimentally inoculated with hepatitis virus obtained during an epidemic. Liver biopsies in two patients, 9 months and 6 months after the onset of the acute hepatitis showed evidence of activity in a late or chronic stage. Thus the existence of a subacute or chronic stage of hepatitis is unquestionable and can account for some of the cases with chronic symptoms.

2. *Psychoneurosis:*—A question still remains, however, as to whether *all* patients with the so-called "characteristic" symptoms and with hepatomegaly actually have a chronic virus infection of the liver. Laboratory tests of hepatic function have not been conclusive; Barker and Capps[1], as well as other workers[4], have found a battery of such tests to be negative in many of their cases and postulate an "inactive form". Pathological studies of the problem have also been inconclusive. Mallory[5] reports studies of biopsy material obtained from soldiers in the Mediterranean Theatre having nonfatal viral hepatitis. His series contained 40 cases which were clinically classified as having "delayed recovery". In fifteen of these, the biopsy was normal; in ten the findings were pathologically doubtful and only fifteen were definitely positive. Among ten other cases classified as "chronic hepatitis without jaundice", seven biopsies were normal, two doubtful and only one positive.

Such frequent negative findings have led some workers to consider the post-hepatitis syndrome as a psychoneurotic manifestation. Caravati[6] and Benjamin and Hoyt[7] have pointed out the similarities of the symptoms to neurotic states. The latter authors also found normal liver tissues in two such patients from whom biopsies were obtained.

Sherlock and Walshe[8], studied twenty soldiers having enlarged livers and symptoms which persisted after clinical recovery from acute hepatitis. These sol-

diers yielded negative results when a battery of liver function tests were performed. Aspiration biopsies were interpreted as normal although scarring in the periportal areas and trivial fatty changes in liver cells were occasionally seen. These workers felt the symptoms to be of psychogenic origin and attributed the palpable hepatic edge to downward displacement rather than to enlargement of the liver.

The data presented in this study was originally submitted to the Mediterranean Theatre Surgeon in 1944 to demonstrate that not all patients diagnosed as "chronic hepatitis" actually had such a disease. Our conclusions were not accepted because they apparently were not in accord, at that time, with the Army policy, which considered most of these patients to be suffering from a chronic viral hepatic infection. We had pointed out that in performing routine physical examinations on many soldiers who were admitted because of wounds, trench foot, etc., it was found that in at least ten per cent of these nonmedical patients the livers could easily be palpated below the costal margin. Some palpable liver edges were two to three finger breadths below the costal margin, yet most of these men had *no* dyspepsia or asthenia. These observations were confirmed by personal conversations with our English and Canadian Medical colleagues, who informed us that a similar number of their seasoned combat troops also had firm, easily palpable livers without any accompanying symptoms.

The lack of correlation between symptoms and hepatomegaly led us to investigate further whether the complaints were on a neurotic basis. Schwartz and Perlmutter[9], in a survey of one hundred twenty-two soldiers, hospitalized in Italy for chronic dyspepsia, found forty-one had been diagnosed as having "chronic hepatitis without jaundice". Of these, only four had any confirmatory laboratory evidence of liver damage. Careful psychiatric survey led to the diagnosis of severe psychoneurosis in seventy-seven per cent. These findings led us to conclude at that time (early 1944) that the symptoms of the syndrome under discussion could not be differentiated from those of a psychoneurotic state. We were also forced to conclude that all patients with firm, easily palpable livers could not be clinically diagnosed as having chronic hepatitis merely because they had accompanying symptoms. Laboratory or pathological evidence is necessary before actual liver infection can be proven to exist in these patients.

Nevertheless, the experience of Capps and Barker[1], as well as Klatskin and Rappaport[2], was amply confirmed by us on many occasions, namely, that patients, who for several months had a symptomatic hepatomegaly without jaundice and without laboratory evidence of liver damage, could suffer a relapse with the occurrence of fever, jaundice, etc. Some of these patients had been considered the worst "neurotics". This occurred with embarrassing frequency in the professional personnel of our own overseas hospital so that by 1945 it was difficult for us to conclude that psychoneurosis alone was the cause. Kalk[10] emphasized that chronic hepatitis could easily be diagnosed as psychoneurosis and warned against this error.

3. *Functional Hepatopathy:*—We have since learned that the syndrome discussed in this paper had been recognized and had puzzled able physicians in the early part of this century. The English students of hepatic diseases, including Davidson[11], Rolleston[12] and Hurst[13] described an "active congestion of the liver" giving rise to the same symptoms of "liverishness", hepatomegaly, and neurotic manifestations described in our cases. One of the conditions causing the active hepatic congestion was called "tropical livers". This syndrome typically occurred in individuals who resided in the tropics and who in the past had malaria, dysentery, yellow fever, typhoid, etc. It was also seen in English troops following their return from the tropics, and was carefully studied by Davidson[11]. The vulnerability of the liver of these patients to a variety of diseases was recognized. On postmortem examination, microscopic studies of the liver of these patients showed no more than dilated capillaries and "cloudy swelling" of the liver cells with occasional mild fatty changes. These workers therefore concluded that the syndrome was due to a functional disturbance of the liver probably caused by active hepatic congestion. Although this explanation of the pathological physiology may not be acceptable, the concept of a functional hepatic disorder as the cause of the lingering debility should be reexamined in light of newer experience.

There is no question that during the recent war, both chronic hepatitis of virus origin and psychoneurotic dyspepsia occurred more frequently than had previously been appreciated. However, in the absence of a specific test for icterogenic virus, the possibility is not eliminated that many cases clinically diagnosed to be in those two categories might actually fall into the third category of having a functional hepatopathy such as the "tropical livers" described by the older clinicians. With this in mind our data concerning this problem has again been reviewed.

Methods and Results

One hundred patients presenting hepatomegaly and the symptoms described above were selected at random on the wards of a military general hospital in the Mediterranean Theatre of Operations. This represents a change in orientation from other studies in which cases of acute hepatitis were followed for chronic sequelae. The histories of our one hundred patients were carefully reviewed to determine whether etiological factors could be established.

In a further effort to evaulate this group of patients we utilized every liver function test available to us at that time. These included total serum proteins, albumin-globulin ratio, icterus index, hippuric acid excretion, cephalin flocculation, serum alkaline phosphatase, bromsulfalein excretion (after administering five mg. per kilogram of body weight), as well as agglutination tests to rule out the enteric and undulant fevers, stool examinations for amebae, and blood smears for malaria. We attempted to use the gallbladder x-ray visualization, after both oral and intravenous administrations of tetraiodophenolphthalein, as an excretory liver function test. X-ray examinations of the stomach and duodenum were done on all patients. Gastroscopy was performed on fifty-three of these individuals. In

twenty-four, there was definite evidence of "superficial gastritis" which one of the authors[14] maintains is closely correlated with the emotional status of the individual.

An analysis of the results showed that only nine of the one hundred cases had laboratory evidence of liver damage; ninety-one had completely negative findings. In order to determine the most probable etiological factors which might have caused the hepatomegaly, a careful history and survey of all recent illnesses in these patients was made. Table I shows the distribution of disease states found in the immediate past history of those patients who had no laboratory evidence of hepatic damage. Since the grouping requires better definition, discussion is included and representative cases are presented to illustrate each type.

TABLE I

ONE HUNDRED CASES OF SYMPTOMATIC HEPATOMEGALY WITHOUT JAUNDICE

Hepatomegaly with laboratory evidence of liver damage	9 cases
Hepatomegaly with no laboratory evidence of liver damage	91 "
Postdiarrheal hepatomegaly	27 "
Postmalnutrition hepatomegaly	14 "
Postjaundice hepatomegaly	31 "
Postinfection hepatomegaly	19 "

Postdiarrheal Hepatomegaly:—Twenty-seven cases in this series had recurrent or chronic diarrhea without a history of ever having had jaundice. The studies of Eppinger[15] during the last war highlighted the occurrence of enlarged livers in patients suffering from severe salmonella diarrheas. However, Havens and Werner[16] showed that acute virus hepatitis can be complicated by *secondary* invasion with salmonella organisms, and since both are probably ingested, their common occurrence in a single patient can well be expected.

In contrast to this latter view concerning acute diarrheas, clinical experience has shown that there are intestinal diseases characterized by *chronic* diarrhea, toxemia, and anorexia in which evidence of hepatic disease has been demonstrated. Such findings were described by Jones and Peck[17] in tuberculous enteritis and recently actual cirrhosis of the liver has been ascribed to this same combination of conditions in ulcerative colitis[18]. It is possible that the hepatomegaly seen in our chronic diarrheal cases is an early state of a slowly reversible change in the liver. Furthermore most of our patients with diarrhea had also had prolonged treatment with sulfonamides, a potential hepatotoxic agent, previous to being hospitalized.

The problem is further confused by the fact that diarrhea is a symptom recognized to be due to the hepatitis virus. It is, however, unlikely that chronic recurring diarrhea is due to a continued virus infection since postmortem studies of fulminant cases of hepatitis showed no enteritis. The chronic phlegmonous enteritis seen in subacute cases is believed by Lucke[19] to be a terminal complication probably secondary to primary liver disease. Case 1 is presented as representative of what we considered a postdiarrheal type.

Case 1:—Lt. W. W., a twenty-seven year old infantry platoon leader, who had been overseas ten months, was admitted to the hospital in November, 1944

because of recurrent diarrhea, weakness, epigastric distress and nervousness. This officer had been in combat for four months when his platoon suffered heavy casualties. Since that time he had lost his previous cool combat efficiency and found that he had to depend upon his sergeant for moral support. He noted the onset of anorexia, nausea, and diarrhea at that time. Because he feared to show nervousness he frequently left his men momentarily to vomit. For two months he manifested symptoms of intermittent diarrhea with occasional bouts of fever. He was hospitalized on two or three occasions and received sulfadiazine treatment each time with only temporary improvement. Jaundice was never noticed. During this period the patient stated that he ate little more than chocolate and coffee. He lost 30 pounds. Shortly before admission his sergeant was killed and he "went to pieces". The diarrhea became persistent but no blood or mucus was noted in the stool. He was very anorectic and belched frequently. Constant parietal throbbing headaches were very troublesome. He found it difficult to fall asleep and was annoyed by nightmares. On November 1st, when he was admitted for study to a clearing station, the liver and spleen apparently were not palpated. No amebae were demonstrated but Shigella paradysenteriae was found in his stool. A cephalin flocculation test was 0/1+. He was treated with sulfadiazine for eight days, followed by twelve days with sulfaguanidine. The diarrhea and the S. paradysenteria in his stool disappeared but the patient's dyspepsia continued. He was evacuated from the field hospital with the diagnosis of "hepatitis without jaundice" because at this time a tender liver edge was palpated one finger breadth below the costal margin. On admission to our hospital the liver edge was palpated between two to three finger breadths below the costal margin. There was no splenomegaly. Serum bilirubin, icterus index, cephalin flocculation, serum alkaline phosphatase, total serum protein, albumin-globulin ratio, and bromsulfalein excretion tests were normal. X-ray of the gallbladder showed poor visualization at first but a test several weeks later was completely normal. A gastrointestinal x-ray was also normal. The patient was transferred to the psychiatric service for treatment of his severe anxiety neurosis. His dyspepsia and other complaints continued and the hepatomegaly persisted unabated while under our observation for three months.

Postmalnutritional Hepatomegaly:—Cases were classified by us as "postmalnutritional" when this seemed to be primary etiologically. It would seem that a marked negative nutritional balance would be rare in a well-fed army. However, in overseas troops the monotony of diet, comprised chiefly of packaged foods, and the anxiety of combat frequently led to prolonged anorexia. Often the fears of having symptoms from eating C rations led to low caloric and particularly low protein intake for many months. In this series fourteen patients had marked prolonged food restrictions, either self-imposed or because of combat conditions.

One confusing factor should be pointed out, namely, that anorexia may actually be caused by a nonicteric virus hepatitis. All of our patients were carefully checked with this in mind. In all cases, the anorexia was first and coincided with

combat conditions or with a diet confined to C rations, so that there seemed no doubt to us as to which came first.

It is interesting to note that anorexia nervosa does not seem to lead to hepatomegaly despite weight loss that sometimes is more severe than that seen among our troops. Reviews of the subject of anorexia nervosa[20] do not even mention hepatic changes. However, many differences exist between anorexia in the tropics and that in civilian life. Practically all of the soldiers had one or two brief attacks of diarrhea or some other infection at one time or another in contrast to the absence of such complications in anorexia nervosa of civilian life. Furthermore, the fact that most of our troops had taken prophylactic atabrine medication, a potential hepatotoxic agent, also distinguished them from a civilian group. These different conditions may well have influenced the symptomatic hepatomegaly seen in our malnourished patients from Africa and Italy.

Meienberg and Snell[21] also attributed the hepatic disorders seen among the American prisoners of the Japanese as due to malnutrition, but a list of the tropical diseases in the history of these patients included malaria, dysentery, and influenza. In all, nineteen of the fifty cases they studied had evidence of hepatic involvement yet only four had ever had acute hepatitis. These findings among soldiers suffering from malnutrition in the tropics stand in direct contrast to those found in displaced personnel in Germany also suffering from severe malnutrition. Sherlock and Walshe[22] could find no evidence of liver disease among the latter. This would suggest that although malnutrition plays a primary role, other factors are also important. Case 2 is included as representative. A biopsy of the liver in this case was reported as normal. Aside from the initial dysentery, no other infection was found.

Case 2:—M. C., a twenty-four year old colored quartermaster soldier who was overseas nineteen months, was admitted to the hospital because of severe postprandial bloating, nausea after fatty meals, and epigastric pain.

Seventeen months previously, this soldier had a bout of severe bloody diarrhea in Africa a few weeks after arriving overseas. At that time, he was acutely ill and his temperature ranged up to 102 degrees. There was no jaundice. After three weeks of hospitalization, during which time he received a long course of sulfonamide therapy, he was discharged to duty. He had no recurrence of diarrhea from that time on, but he continued to feel very weak and complained of severe postprandial distress, especially after fatty foods. Because of this he was assigned to light company duty. His appetite was capricious and he ate only bread and candy for long periods of time. Four months later, he was hospitalized again for the same complaints. He was discharged after a short rest without any relief of symptoms. Because of a further weight loss of 15 pounds and continued dyspepsia after eating, he was admitted to our hospital. The patient denied having had any diarrhea for over a year.

He stated that formerly his natural disposition had been amiable and generally without cares or worries, but since his illness had continued without relief for more than a year he was becoming "nervous". Physical examination revealed a very thin, apprehensive individual. A hard, tender liver edge was felt one finger breadth below the costal margin. No spleen was felt. Tests for serum bilirubin, cephalin flocculation, and sedimentation rate were normal. The serum alkaline phosphatase was normal and the bromsulfalein test was within normal limits. The stools were negative for amebae. Gastrointestinal series was negative, but a gallbladder study, both by oral and intravenous route, revealed complete nonvisualization.

An exploratory laparotomy revealed a normal gallbladder. The liver appeared grossly normal to the surgeon. A biopsy of the liver was taken and the operation was terminated without any other procedure. The pathological report by Dr. Tracy Mallory in the 15th General Medical Laboratory, corroborated our pathologist's diagnosis that the liver biopsy sections were entirely normal.

One month after operation a repeated gallbladder series showed normal function. The cephalin flocculation was 0/0. One serum alkaline phosphatase determination was 6.3 units (normal=6). Two months after the operation, despite high protein diet, the patient's symptoms were unchanged. His liver was still easily palpable 1½ fingers below the costal margin and was apparently tender. The cephalin flocculation test, serum alkaline phosphatase and bromsulfalein test were all normal. He was still extremely anorectic, weak, apprehensive, dyspeptic, and tremulous. He was sent to the Zone of the Interior because of his marked neurasthenia and anxiety state.

Postjaundice Hepatomegaly:—After selecting these one hundred patients at random it was impossible to tell from the symptoms or physical signs which patient had previously had jaundice without the patient having indicated it in his history. Only forty of the one hundred cases were found to have a preceding history of acute hepatitis with jaundice. Nine of these had persistent abnormal liver function tests several months after the acute icteric hepatitis subsided. Thirty-one presented a persistent hepatomegaly with the above mentioned symptoms *without* laboratory evidence of abnormal liver function. It is possible that, as demonstrated by Neefe[23], that the use of the newer thymol turbidity and flocculation tests would have added some additional patients to the former group, but our experience coincides with that of many other investigators in this field, namely, that positive laboratory evidence of parenchymal involvement is not common among such patients. We were able to obtain liver biopsies in two such cases and both were reported as "normal liver tissue". As was mentioned before it was in this type of hepatic disturbance that Mallory[5] could find no evidence of abnormal histological structure in the majority he studied.

Since previous investigations of this problem have been designed to study the sequelae of acute hepatitis, evidence has been heavily weighted in favor of the view that patients presenting the syndrome of hepatomegaly with anorexia, dys-

pepsia and asthenia, had a delayed convalescence of a chronic virus hepatitis. The present study, viewed with a more general perspective, reveals that only about two-fifths of the patients presenting this syndrome previously had acute icteric hepatitis and makes it difficult to believe first that all the other patients (three-fifths) had had acute hepatitis without jaundice and, secondly, that such cases were more susceptible to a chronic form.

The authors were all agreed that the nine patients with laboratory evidence of hepatic parenchymal damage were definitely cases of chronic hepatitis following acute hepatitis with jaundice. Clinically, we found it was impossible to differentiate them from those without laboratory evidence of parenchymal involvement thus demonstrating the fallacy of depending merely on history, symptoms, and hepatomegaly for a diagnosis.

Many of our patients, classified as having a postjaundice hepatomegaly, also had a previous history of chronic diarrhea or prolonged anorexia similar to the patients in the preceding two groups already mentioned. This fact might well explain the statistical differences in complications found after epidemic jaundice in well-nourished civilians and in tropical conditions.

An example of the nine cases with laboratory evidence of parenchymal involvement is not included since these are common enough in the literature. Case 3 is presented to show the syndrome under discussion soon after the acute hepatitis subsided.

Case 3:—W. D., a nineteen year old white rifleman, was hospitalized on the surgical service for a sprained ankle. His past history revealed that shortly after arriving in Italy, he began to have frequently recurrent attacks of diarrhea consisting of four to five loose, large, watery, brown stools a day. This persisted for over a period of five months. The stools contained neither blood nor mucus and he was always afebrile. Sulfonamides caused only temporary subsidence of the diarrhea. Although his appetite had been good he lost ten pounds. Shortly after his admission to the hospital he was transferred to the medical service because he had a recurrence of his diarrhea and an irregular fever rising to 104 degrees. At this time, during his first week in the hospital, a tender liver was palpated one finger breadth below the costal margin. The icterus index was 5, the cephalin flocculation was 1+/3+. However, by the end of the week the icterus index had risen to 41 and the diagnosis of acute hepatitis with jaundice was established.

Throughout the early weeks of hospitalization, both the jaundice and the diarrhea persisted. Repeated stool examinations, proctoscopic examination, x-ray of stomach, small intestine and colon, failed to reveal any abnormality. Because of severe nightmares, continued asthenia and anorexia, phychiatric consultation was necessary. Transfer to the psychiatric ward for treatment was advised after the jaundice subsided because of the intensity of his anxiety. Six weeks later, the patient had only slight dyspeptic symptoms and the diarrhea had ceased. The liver edge, which was firm, sharp, and slightly tender, could be flipped two finger

breadths below the costal margin. At this time, all the laboratory tests, including sedimentation rate, icterus index, cephalin flocculation, serum alkaline phosphatase, bromsulfalein excretion, total serum protein and albumin-globulin ratio, plus x-ray visualization of the gallbladder, were normal. The patient was transferred to limited duty. We were able to follow this patient for four more months. He continued to present a persistent hepatomegaly, but most of his symptoms subsided after he was assigned to noncombat duty.

Case 4 is presented to illustrate the neuropsychiatric aspects of a long standing illness following hepatitis with jaundice.

Case 4:—G. H., a twenty-three year old white combat corporal had been overseas for twenty-eight months. He was originally hospitalized in Italy for infectious hepatitis with jaundice. Two months later, he was evacuated to Africa because of persistence of dyspepsia and hepatomegaly although the jaundice had disappeared. After another month of hospitalization, he was returned to duty on the Anzio beachhead. One week after he arrived at the beachhead, vomiting, fatty food intolerance, and epigastric distress reappeared. He was again hospitalized at Anzio but was shortly returned to duty. A few weeks later, he was evacuated for the second time to a rear echelon station hospital. This time he was placed on "hepatitis ward" because the liver was palpably enlarged. The symptoms of anorexia and vomiting persisted despite bed rest and a high protein diet. On palpation the liver was noted to be two finger breadths below the costal margin. All the laboratory tests during that hospitalization, including the erythrocyte sedimentation rate, icterus index, serum alkaline phosphatase, cephalin flocculation and bromsulfalein excretion, were normal. He was diagnosed as having latent "chronic hepatitis without jaundice" and evacuated to this hospital.

All the above findings were corroborated by us. X-ray visualization of the gallbladder, stomach and duodenum were normal. The gastric mucosa, as seen through the gastroscope, was normal. There was no history or signs of alcoholism, malaria or dysentery. This patient ate his high protein diet well but despite this the hepatomegaly did not decrease and his dyspepsia persisted. Because of a marked anxiety about his enlarged liver, a psychiatric consultation was obtained and the psychiatrist recommended transfer to the Zone of the Interior because of a very severe "anxiety state".

Postinfectious Hepatomegaly (including Postmalaria Hepatomegaly):—The hepatomegalic syndrome was also seen after various types of infections. There were nineteen such cases in this series, thirteen of which occurred after malaria. The occurrence of a persistent hepatomegaly after a malarial infection has striking similarities to the hepatopathy remaining after acute infectious jaundice. During the active phase of the disease the plasmodium can cause an acute hepatitis without jaundice as evidenced by the frequent finding of enlargement of the liver and by the abnormal liver function tests. With adequate treatment of the malaria, laboratory evidences of hepatic dysfunction disappear within several weeks and

yet in some cases hepatomegaly and liver symptoms persist. Case 5 is representative of this type. It was *after* treatment of the malarial parasitism with atabrine, and *after* the laboratory tests for hepatic dysfunction returned to normal, that the syndrome manifested itself clearly. Without a specific test for the hepatitis virus, it was impossible to rule out its coexistence in this patient, but this seems unlikely. Why some patients with malaria develop hepatomegaly, and others with a more severe and more relapsing type do not, is not known. From the pathological viewpoint, the medical literature at present is as vague about the nature of the hepatomegaly in nonfatal malaria as it was previously concerning the postjaundice type. One such case, illustrated in Weiss' textbook[24], shows pigment deposition with a marked edema of the liver parenchyma but no cellular or stroma changes.

In this respect a clinical study[25] of nonalcoholic cirrhosis of the liver occurring in Lebanon and Syria is informative. In these countries cirrhosis is seen chiefly among farmers living on low protein diets and manifests itself in young people (twenty per cent are less than twenty years old) after a long course for many years characterized by transient hepatic enlargement, recurring febrile attacks with jaundice, and chronic biliousness. The author noted that chronic malaria and dysentery, especially a combination of the two, are important factors in the etiology of the cirrhosis since that disease is uncommon in districts where these diseases are more promptly treated.

Not only malaria and dysentery but other infections gave rise to this syndrome. Most informative to us, were six patients who developed the hepatomegaly in our hospital after they contracted virus pneumonia and phlebotomus fever. Four of these were medical officers and nurses from our own organization. Liver enlargement developed in all of these patients while they were convalescing. Case 6 illustrates this. Sabin's[26] control study of experimentally induced pappataci fever in well-nourished volunteers in the United States reports the absence of either hepatomegaly or laboratory evidence of liver involvement in any of his cases. We also saw no persistent hepatomegaly in many sand-fly fever patients without a previous history of gastrointestinal symptoms and poor nutrition. Although all of our patients were returned to duty after one month of bed rest, the hepatomegaly and mild symptomatology persisted for many months in spite of repeatedly negative x-ray and laboratory findings. One of these patients, a medical officer, was refused re-enlistment into the regular army two years later because his markedly enlarged liver was found on physical examination.

We doubt whether these observations about the frequency of palpable livers would have been made had we not been made "liver conscious" by our study of this problem. More observations are needed in civilian life, particularly among peoples coming from semitropical environments or from countries where nutritional standards are low and diarrhea, malaria, etc., are common.

Case 5:—M. H., a twenty-three year old infantry squad leader, who had been overseas nineteen months, was admitted to the hospital on August 8, 1944 because of weakness, vomiting, biliousness and a heavy sensation in the right upper quadrant. There was no history of jaundice, but this sergeant had had five previous attacks of malaria treated with atabrine during his foreign service. For three weeks before admission to this hospital, he had noted lack of drive, weakness and anorexia, the latter leading to marked loss of weight. He belched frequently. Moderate emotional instability was elicited during a psychiatric interview. The patient was afebrile during his first month of hospitalization. During this period atabrine suppressive therapy was stopped for the first time since he was overseas. Despite this, repeated blood smears failed to show any plasmodia. The sedimentation rate, icterus index and cephalin flocculation tests were normal, but the serum alkaline phosphatase was elevated to eight units (our normal at that time was six). The liver and spleen were *not* felt. At the end of a month of bed rest with a high protein diet, the patient had gained eight pounds and no longer felt weak. One week after feeling better he again began to have anorexia and "lost his pep" completely. On September 12th, he had a severe chill. The splenic tip became palpable and plasmodium vivax was then found in a blood smear. At that time, the liver again began to enlarge and three weeks later had reached two finger breadths below the costal margin. The cephalin flocculation rose to 3+/4+ immediately after the acute attack but returned to normal in three weeks. Four weeks later the bromsulfalein test was normal. The serum alkaline phosphatase continued to remain elevated. He was kept under observation and on atabrine therapy for a total of three and one-half months until he was evacuated to the Zone of the Interior because he still had asthenia, mild abdominal distress, fatty food intolerance, marked neurasthenia and a persistent hepatomegaly despite repeated negative liver function tests.

Case 6:—W., a twenty-five year old nurse who had been overseas thirteen months was admitted to the hospital with a fever of 104 degrees that had started suddenly after a severe nonshaking chill. She complained of severe headaches and prostration. In addition, there was marked muscle aching particularly in the lumbar region and behind the eyes. This occurred during the course of an epidemic of three day grippal-type of infection which was clinically diagnosed as pappataci fever, current in Naples at the time. On admission the examination was essentially negative, aside from the signs attributed to the fever. There was no jaundice and the liver and spleen were not felt. The blood showed a normal count with slight neutropenia but no abnormal lymphocytes were seen. The urine was negative. No bile was found. After three days of conservative therapy the fever completely subsided. The patient continued to remain extremely weak, had no appetite, and complained of a "bloated feeling" and moderate nausea after eating. On the third day, the liver and spleen still were not felt, the icterus index was six, and the cephalin flocculation test, sedimentation rate, serum alkaline phosphatase were negative. On the following day the bromsulfalein test also showed abnormal retention.

A check of the past history revealed that the patient had been healthy except that for three months preceding the present illness she had been complaining of a mild diarrhea and lack of appetite. Since she was worried about her fiancé who was in combat, her friends joked about it. After losing fifteen pounds of weight, she applied for a physical examination but on two occasions nothing was found. These symptoms first appeared in April at a time when virus hepatitis was not prevalent and the hospital was not active. The present illness occurred in July.

On the fifth day after the onset of the illness, an enlarged tender liver was found. The hepatomegaly persisted in spite of two months of bed rest. With a high protein, high carbohydrate diet and supplementary vitamins she regained ten pounds in weight, and was returned to duty feeling much improved. However, she still became fatigued easily and noticed that overeating led to a "bloated abdomen" and belching. Four months later the tender hepatomegaly was still present although all our liver function tests continued to be negative.

Discussion of Results

Under the conditions found during wartime in an overseas military environment, persistent hepatomegaly (without jaundice) and symptoms that can be characterized as "liverishness" occurred so commonly, that it was comparatively easy for the authors to collect one hundred cases on the wards of a fifteen hundred bed hospital in a relatively short period of time. Due to the common occurrence of two other prevalent wartime conditions, namely, acute infectious hepatitis with jaundice and also psychoneurosis, two views have been expressed, namely, that these two conditions were directly involved as causes of the hepatomegaly and symptoms. We feel that neither view completely explains the entire situation, since both laboratory tests and pathological studies are repeatedly reported as "normal". In many cases, the evidence is against chronic infection. Nor can the diagnosis of psychoneurosis be the only explanation since in quite a number there is an increased hepatic vulnerability to further toxic action.

In searching for clues for a possible etiology, our attention was constantly directed to three factors, namely: (1) negative nutritional balance, (2) a toxic-infectious agent with acute hepatotoxic potentialities, and (3) emotional instability. This triad constantly appeared in most cases in varying degrees. These individual factors were so closely integrated that a clear cut separation into each category was often impossible and, therefore, a consideration of each factor by itself was incomplete. There is no question that a *negative nutritional balance* was common among soldiers. As it was pointed out before, the anxiety of combat and the monotony of having to eat packaged foods, led to anorexia and a great many soldiers consumed a low caloric intake. To this can also be added the loss of nutrition through the frequent occurrence of attacks of diarrhea of unknown origin. A large proportion of the patients with hepatomegaly stated that they had consumed insufficient food or that they had had recurrent diarrheal attacks, or both, prior to the onset of symptoms or the discovery of the enlarged liver.

The toxic infectious agents which we have found as precipitating factors in bringing the patient to the medical department were numerous. Acute mild upper respiratory infections, virus pneumonia, streptococcal pharyngitis, or pappataci fever were occasionally associated with a symptomatic hepatomegaly which lasted several weeks to months after the infections subsided. Also, it would seem that malarial parasites and the hepatitis virus might well similarly act as toxic-infectious agents leading to subsequent hepatopathy in a fashion similar to the infections just enumerated. The most chronic hepatomegalies were found in patients in whom both malnutrition and an infectious agent coexisted. For instance, we have noted the onset of hepatomegaly during an acute primary bacillary (Shigella) dysentery and the hepatomegaly persisted for some time after the diarrhea subsided. The studies of Eppinger[15], emphasizing the occurrence of enlarged livers in patients suffering from severe salmonella diarrheas has not been entirely disproven merely by demonstrating that virus infection can coexist. It is possible that the hepatomegaly, which we are describing, may be the early stage of a reversible metabolic change in the liver and if the malnutrition and toxic condition would have persisted, these changes might have eventually led to hepatic degeneration.

A third factor, *emotional tension*, was also commonly found. It has appeared to us that this was one of the most important causes in the production of a negative nutritional balance. It not only created a decreased food intake through "nervous anorexia" but it also decreased the food absorption through "nervous diarrhea" which only ceased when anxiety was alleviated by reclassification of the soldier to noncombat duty. It often recurred when a patient who had been symptom-free while in the hospital, prepared to leave for combat duty. Psychogenic factors played another role in addition to those just enumerated, namely, they led to an accentuation of the symptomatology in some patients with hepatomegaly to a point where sometimes the anxiety seemed to be the chief condition.

For the most part, after careful study of each case it was difficult to attribute the major role to any single one of the factors. Rather, a synergistic action of all seemed to start and perpetuate a vicious cycle which produced the hepatomegaly without jaundice and the symptoms. The caloric intake was limited by anorexia or in others, the absorption of food was decreased by the diarrheal states. With the nutritional reserve of the liver thus depleted, it was more easily affected by any toxic or infectious agents which included the infective agent causing diarrhea, the jaundice virus, or any other intercurrent infection. The combination of hepatic malnutrition and hepatotoxic agent led to the liver enlargement with an accompanying dyspepsia and asthenia, both of which persisted after the acute causes were removed. The symptoms produced an emotional instability or intensified a preexisting one and perpetuated the cycle.

All these nonspecific considerations seem to reemphasize the possibility that a nonspecific functional hepatopathy can occur. This is in line with the concept of "tropical livers" accepted by leading clinicians at the beginning of this century.

What the pathological physiological mechanism occurring in the liver in such cases may be, is not known.

A review of literature reveals that this inability to explain the mechanism of suspected functional liver disturbances is not uncommon. For instance, in 1935 Rozendaal, Comfort, and Snell[27] studied cases with slight and latent jaundice to "learn something about those many patients who claim to be bilious, liverish, or toxic, but in the examination of whom the usual tests of hepatic function fail to show any sign of disease". These observers collected forty-eight cases with elevated blood bilirubin in whom demonstrable evidence of hematologic, liver, or gallbladder diseases were absent. Eight had completely negative examinations and twenty-three were suffering from a functional nervous disorder. They concluded that "some patients who complain of being bilious actually have slight hepatic dysfunction" and although "it is not clear that all symptoms are actually due to hepatic dysfunction, it is probable in some instances that the hepatic dysfunction may be only one of the manifestations of a widespread sympathetic or toxic reaction". In favor of the latter, they cited evidence that hepatic dysfunction occurs in migrainous patients and suggest that a sympathetic nervous system storm, may provoke both hepatic dysfunction and the bilious headaches.

In more recent literature there are other descriptions of clinical syndromes suggesting liver dysfunction unexplained by chronic virus infection or psychoneurosis. In this respect the findings of Salter, Klatskin and Humm[28] are interesting. These workers studied forty-eight American soldiers with gynecomastia who had been prisoners of war in the Philippines and in Japan. A survey of the histories of these patients for possible liver involvement revealed that twenty-five had had acute hepatitis and twenty-three gave no such history. In the former group, five were found to have residual hepatomegaly and nine had residual impaired liver function. In the group in which no history of liver disease was obtained, four had residual hepatomegaly and two had impaired liver function. Furthermore, in the latter group, two had spider nevi and twelve had palmar erythema. The authors could offer no explanation for these hepatic findings which were seen three months after the soldiers were released from prison.

Not only are clinical studies indecisive concerning the nature of the hepatic dysfunction, but pathological studies are also indefinite. Davidson[11] and Rolleston[12] attributed the syndrome of "tropical livers" to an "active congestion" of the liver occurring in susceptible people after overeating, excess physical exercise, and climate changes. These observers were cognizant of a fact (recently reemphasized by Capps and Barker) that exercise quickly led to enlargement of the liver and thus were influenced to postulate that a vascular congestion took place. Another explanation for hepatomegaly was proposed by Roessle[29] and Eppinger who studied the hepatomegaly following diarrheas in German troops in World War I and attributed the liver changes to an intralobular hepatic edema. These workers believed that this represented a true "serous hepatitis" pathologically significant in the production of

cirrhosis even in the absence of parenchymal changes or cellular infiltration. On the other hand the concept of serous hepatitis is refuted by Keschner and Klemperer[30] who view this finding as due to an increased capillary permeability of the sinus endothelium encountered in a variety of diseases.

Pathologists have not adequately explained the cause of hepatomegaly in other disease states. A good example of this is found in diabetes mellitus. The hepatomegaly commonly seen in diabetics is usually stated to be due to fatty infiltration but actually, students of this problem (see reviews by Joslin[33] and Bockus[31]) have found no significant pathological or chemical alterations in many such cases. Krarup and Iversen[32] suggest that "edematous choking of liver cells" is probably the cause of diabetic hepatomegaly and Joslin's coworkers suggest that hepatic "cellular hydropic degeneration with fluid retention" may be the basis for these enlarged livers.

Until cellular pathologists can further study these problems in the syndrome now under discussion as well as in other clinically described conditions, such as diabetic hepatopathy, or the hepatomegaly of prisoners with gynecomastia developing after liberation from Japanese camps, it is important that physicans explore all the clinical possibilities. Our experience would suggest that the majority of our patients fall into a category of having a functional "hepatopathy" caused by a combination of circumstances discussed rather than chronic virus hepatitis or merely an anxiety complex.

We have recently seen this same problem concerning symptomatic hepatomegaly occurring among the malnourished Puerto Ricans who have migrated to New York.

Summary

(1) A chronic syndrome characterized by hepatomegaly without jaundice and accompanied by symptoms of anorexia, dyspepsia, asthenia and neurotic manifestations was seen in large numbers of American soldiers in the Mediterranean Theatre of Operations.

(2) The greater majority (ninety-one per cent) had no evidence of hepatic disease when studied by the usual laboratory tests. Pathological studies of liver biopsy sections reported in the recent literature disclosed only a relatively small percentage having positive findings.

(3) Clinically there is evidence to show that this syndrome may be a functional hepatic disorder following a variety of insults to the liver.

(4) The syndrome followed nutritional deficiency usually associated with accompanying toxic-infectious hepatopathic agents. The former resulted from chronic diarrhea and prolonged anorexia. The toxic-infectious agents included various factors such as virus, salmonella, shigella, and malarial infections and possible atabrine and sulphonamide medication. Emotional factors were closely interwoven in the pattern.

(5) Until specific tests for the virus of infectious hepatitis are available, it is difficult to evaluate statistically the role of the hepatitis virus in the production of this chronic hepatic picture. Only forty per cent of the patients in this series ever had manifest acute hepatitis.

(6) Cases of chronic virus hepatitis cannot be differentiated from those having a functional hepatopathy by clinical signs or symptoms. Liver biopsies, virus tests, and more sensitive liver function tests are needed to determine the difference and hence the prognosis in each case.

REFERENCES

1. Barker, M. H. Capps, R. B. and Allen, F. W.: Chronic Hepatitis in the Mediterranean Theater: A New Clinical Syndrome. J.A.M.A. **129**:653, 1945.
   Capps, R. B., Shorov, V. M. and Barker, M. H.: The Diagnosis of Infectious Hepatitis. J.A.M.A. **134**:595, 1947.
2. Rappaport, E. M. and Klatskin, G.: Relapses and Recurrences of Infectious Hepatitis. Rev. Gastroenterol. **14**:17, 1947.
   Klatskin, G. and Rappaport, E. M.: Late Residuals in Presumably Cured Acute Infectious Hepatitis. Ann. Int. Med. **26**:13, 1947.
3. Neefe, J. R.: Recent Advances in the Knowledge of Virus Hepatitis. M. Clin. North America. 1407-1443. (Nov.), 1946.
   Neefe, J. R., Gellis, S. S. and Stokes, J., Jr.: Homologous Serum Hepatitis and Infectious (Epidemic) Hepatitis. Am. J. Med. **1**:3, 1946.
4. Tumen, H. J. and Cohn, E. M.: The Validity of Laboratory Evidence in the Diagnosis of the Sequelae of Acute Hepatitis. Gastroenterology. **12**:92, 1949.
   Neefe, J. R.: Results of Hepatic Tests in Chronic Hepatitis Without Jaundice. Gastroenterology. **7**:1, 1946.
5. Mallory, T. B.: The Pathology of Epidemic Hepatitis. J.A.M.A. **134**:655, 1947.
6. Caravati, C. M.: Post Hepatitis Syndrome. South. M. J. **37**:251, 1944.
7. Benjamin, J. E. and Hoyt, R. C.: Disability Following Post-Vaccinal (Yellow Fever) Hepatitis. J.A.M.A. **128**:319, 1945.
8. Sherlock, S. and Walshe, V.: Post Hepatitis Syndrome. Lancet. **2**:482, 1946.
9. Schwartz, I. R. and Perlmutter, M.: Chronic Dyspepsia in the Mediterranean Theatre. Gastroenterology. **6**:21, 1946.
10. Kalk, H.: Klinische Untersuchungen Über die Frage des latenten Leberschadens. Deutsche Med. Wchnschr. **58**:1078-1119, 1932.
11. Davidson, A.: Tropical Liver in Albutt, T. C. and Rolleston, H. D. System of Medicine. **2**:574, 1907.
12. Rolleston, H. and McNee, J. W.: Diseases of the Liver, Gall Bladder and Bile Ducts. 3rd Edition. Macmillan, London. 1929.
13. Hurst, A. F.: On Being Liverish. Libman Anniversary Volume. **2**:573, 1932.
14. Halsted, J. A., Schwartz, I. R., Rosen, S. R., Weinberg, H. and Wyman, S. M.: Correlated Gastroscopic and Psychiatric Studies of Soldiers with Chronic Non-Ulcerative Dyspepsia. Gastroenterology. **7**:177, 1946.
15. Eppinger, H., Kannitz, H. and Poppe, H.: Die Seröse Entzundungen. Vienna, Julius Springer, 1915.
16. Havens, W. P., Jr. and Werner, H. A.: Infectious Hepatitis Complicated by Secondary Invasion with Salmonella. J. Clin. Invest. **25**:45, 1946.
17. Jones, J. M. and Peck, W. M.: Incidence of Fatty Liver in Tuberculosis with Special Reference to Tuberculous Enteritis. Arch. Int. Med. **74**:371, 1944.
18. Comfort, M. W., Bargen, J. A. and Morlock, C. G.: Association of Chronic Ulcerative Colitis with Hepatic Insufficiency. M. Clin. North America. **22**:1089, 1938.
    Bockus, H. L.: Gastroenterology. Vol. II, p. 596. W. B. Saunders Co., Philadelphia, 1944.
19. Lucke, B.: The Pathology of Fatal Epidemic Hepatitis. Am. J. Path. **20**:471, 1944.
20. Escamilla, R. F. and Lisser, H.: Simmonds Disease and Its Differentiation from Anorexia Nervosa. J. Clin. Endocrinol. **2**:65, 1942.
21. Meienberg, L. J. and Snell, A. M.: Nutritional Deficiency as a Probable Cause of Hepatic Damage in Repatriated Prisoners of War. Gastroenterology. **7**:430, 1946.
22. Sherlock, S. and Walshe, V.: Effect of Undernutrition in Man on Hepatic Structure and Function. Nature. **161**:604, 1948.
23. Neefe, J. R. and Reinhold, J. G.: Laboratory Aids in the Diagnosis and Management of Infectious (Epidemic) Hepatitis. Gastroenterology. **7**:393, 1946.

24. Weiss, S.: Diseases of the Liver, Gall Bladder, Ducts and Pancreas. Paul Hoeber, New York, 1935.
25. Yeni Komshian, H. A.: Non-Alcoholic Cirrhosis of the Liver in the Lebanon. J.A.M.A. **103**:660, 1934.
26. Sabin, A. B., Philip, C. B. and Paul, J. R.: Phlebotomus (Pappataci or Sandfly) Fever. J.A.M.A. **125**:693, 1944.
27. Rozendaal, H. M., Comfort, M. W. and Snell, A. M.: Slight and Late Jaundice. J.A.M.A. **104**:374, 1935.
28. Salter, W. T., Klatskin, G. and Humm, D.: Gynecomastia Due to Malnutrition. Trans. A. Am. Physicians. **59**:120, 1946.
29. Roessle, R.: Entzündurigen der Leber in Henke, F. and Lubarsch, O. Handbuch der Speciallen pathologischen Anatomie und histologie. Julius Springer, Berlin. **5**:250, 1930.
30. Keschner, H. W. and Klemperer, P.: Frequency and Significance of Hepatic Edema. Arch. Path. **22**:583, 1936.
31. Bockus, H. L.: Gastroenterology. Vol. III, p. 391. W. B. Saunders Co., Philadelphia, 1944.
32. Iversen, P. and Krarup, N. B.: Steatosis Hepatis Behandlet med. Vitamin B_1. Ugesk. f. laeger. **103**:66, 1941.
33. Marble, A., White, P., Bogan, J. K. and Smith, R. M.: Enlargement of Liver in Diabetic Children. Arch. Int. Med. **62**:740, 1938.

PANCREATIC LESIONS IN HODGKIN'S DISEASE*

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The more comprehensive articles in the literature have been reviewed to determine the incidence of pancreatic involvement during Hodgkin's disease.

Hoster and Dratman[1], in their recent review, state that the pancreas is not immune to infiltration, and they emphasize the fact that extensive involvement of this organ by Hodgkin's disease may occur without the development of diabetes.

Simonds[2] quotes several authors as to reported lesions in the pancreas. No statistics are given.

Symmers[3] and Wallhauser[4] make no reference to pancreatic lesions.

Jackson and Parker[5] state that in fifty-nine of their cases of Hodgkin's granuloma, autopsy showed the pancreas to be involved in eight instances (13.5 per cent); in eleven, or 41 per cent, of their twenty-seven cases of Hodgkin's sarcoma the pancreas was involved.

TABLE I

Case	Age	Sex	Duration of Disease	Treatment	Pancreatic Involvement
1	67	F	13 mo.		Acute pancreatitis
2	22	M	18 mo.	x-ray	Hodgkin's disease of pancreas
3	23	M	28 mo.	x-ray	Hodgkin's disease of pancreas
4	23	M	5 mo.	x-ray	Interlobular fibrosis
5	23	M	21 mo.	x-ray	Hodgkin's disease of pancreas, with interlobular fibrosis
6	33	M	3 yrs. 5 mo.	x-ray	Interlobular fibrosis
7	30	F	7 yrs. 2 mo.	x-ray; Nit. Must.	Active Hodgkin's disease involving interlobular septa
8	60	F	4 mo.	x-ray; Nit. Must.	Diffuse Hodgkin's disease
9	44	F	2 yrs. 6 mo.	x-ray; Nit. Must.	Interlobular fibrosis
10	44	M	8 yrs.	x-ray; Nit. Must.	Acute pancreatitis

Landolt[6] reports a case of Hodgkin's disease accompanied by acute hemorrhagic pancreatitis and lithiasis of the pancreas. He concludes that the pancreatitis resulted from the lithiasis, and emphasized the rarity of Hodgkin's disease and concomitant acute hemorrhagic pancreatitis. He further states that "one might imagine that the pancreatitis had its origin in an alteration in the pancreas due to lymphogranuloma, but no support for this was found at autopsy".

In view of the meagre statistics as to involvement of the pancreas by Hodgkin's disease, we decided to review carefully our autopsy material in an effort to augment these statistics.

Material and Methods of Study:—Our data are taken from the hospital records of forty-four patients who died of Hodgkin's disease during the past six years at St. Vincent's Hospital, New York City, and who were autopsied.

*From the Hodgkin's Disease Research Laboratory, St. Vincent's Hospital, New York, N. Y. Supported in part by grants from the National Cancer Institute of the U. S. Public Health Service, the American Cancer Society, and the Damon Runyon Memorial Fund.

The diagnosis of pancreatic disease was based on examination of routine sections prepared at the time of autopsy. In most instances involvement of the pancreas was grossly obvious.

Instances of peripancreatic disease were excluded from this analysis.

Findings:—Observations are summarized in the table.

Two types of lesions were found, one acute and the other chronic. The first type, noted in two of the ten autopsied cases, was in every way similar to and

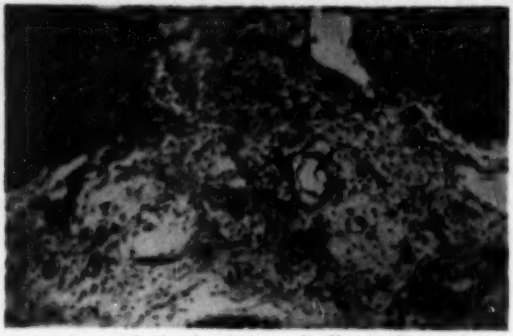

Fig. 1—Low power photomicrograph showing increase in fibrous tissue, edema and infiltration with reticuloendothelial cells and occasional lymphocytes.

indistinguishable from the usual pathologic picture of nonhemorrhagic, acute pancreatitis with fat necrosis; in neither case was the pancreas per se invaded by Hodgkin's disease. In Case 1 macroscopic examination demonstrated the presence of an occlusive coagulum within several of the ducts.

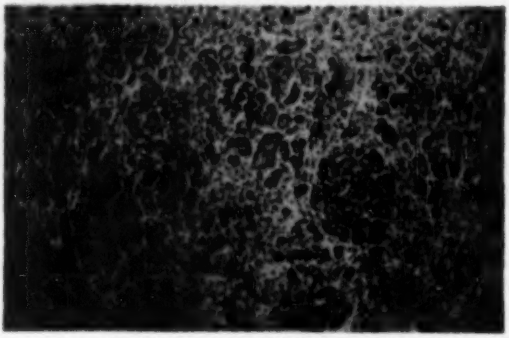

Fig. 2—(Case 8). Low power microphotograph showing diffuse cellular infiltration of the entire pancreas. Some of these cells are of the Sternberg-Reed type.

In three cases the findings in the pancreas were quite clearly Hodgkin's disease processes, being in every way similar to the disease processes elsewhere present in the body. The lesion was either the usual nodular replacement of normal tissue or fibrosis of the interlobular septa. In the latter case the septa were thickened, due to edema and to an infiltrate of mononuclear cells, among which Sternberg-Reed cells were recognized (Fig. 1).

In only one pancreas (Case 8, Fig. 2) was there diffuse involvement of the intralobular portion of the pancreas as well as of the interlobular septa. In this instance, the cellular components were chiefly mononuclear reticulum cells with a scattering of Sternberg-Reed cells.

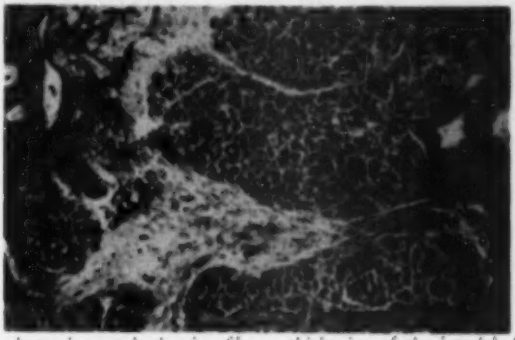

Fig. 3—Low power photomicrograph showing fibrous thickening of the interlobular septa.

In three instances the lesions in the pancreas consisted of widespread, dense, fibrous thickening of the interlobular septa, devoid of cellular infiltrate (Fig. 3).

Discussion

At autopsy, lesions in the pancreas were found in ten of forty-four persons who had died of Hodgkin's disease. In two instances there was typical acute pancreatitis though neither patient had shown clinical evidence of pancreatitis. In both instances the acute pancreatitis had occurred as a terminal complication of long-standing, progressive Hodgkin's disease. The cause of the pancreatitis remains obscure.

Case 8 of our series was unique. The pancreatitis was of a kind typical of Hodgkin's disease and involved both the intralobular and interlobular connective tissue of the entire pancreas. Pancreatic dysfunction had not been clinically evident. No laboratory tests had been done to show such a dysfunction, however, since pancreatitis was not suspected. The usual anatomical involvement of the pancreas by Hodgkin's disease, though it may be extensive, is not uniformly diffuse. The disease apparently spreads to the organ in a retrograde manner from secondarily-involved peripancreatic tissue. The process terminates with a production of connective tissue, leading to thickening of interlobular connective tissue. Since all but one patient received x-ray alone, or x-ray and nitrogen mustard, it would be reasonable to assign some role to these therapeutic procedures as partial explanation for the subsidence of the active pancreatitis in some of the cases.

Summary

Pancreatitis occurs in patients suffering from Hodgkin's disease.

It is usually chronic.

The process may become inactive as the result of therapy.

Clinical manifestations are not clear-cut.

In an acute form it occurs as a complication of terminal Hodgkin's disease.

REFERENCES

1. Hoster, H. A., Dratman, M. B., Craver, L. F. and Rolnick, H. A.: Hodgkin's Disease. Cancer Research, **8**:1-48, (Jan.), and **8**:49-78, (Feb.), 1948.
2. Simonds, J. P.: Review of Hodgkin's Disease. Arch. Path. **1**:394-430, 1926.
3. Symmers, D.: Lymphoid Diseases. Arch. Path. **45**:73-131, 1948.
4. Wallhauser, A.: Hodgkin's Disease. **16**:522, (Oct.), and **16**:672, (Nov.), 1933.
5. Jackson, H., Jr. and Parker, F., Jr.: Hodgkin's disease and allied disorders. Oxford University Press, New York, 1947, p. 177.
6. Landolt, R. F.: Lymphogranulomatosis associated with acute hemorrhagic pancreatitis. Klin. Wchnschr. **22**:36, (Jan.), 1943.

MESENTERIC THROMBOSIS OF MIDJEJUNUM WITH RESECTION AND RECOVERY

(Case Report)

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The problem of mesenteric thrombosis continues to be a difficult one, both as regards diagnosis and management.

Johnson and Baggenstoss[1], in recently reporting a study of 99 cases of occlusion of mesenteric veins encountered at the Mayo Clinic from 1911 to 1945, give the average length of life after onset of symptoms, in cases in which infarction occurred, as 6.8 days.

The following report is being offered as an example of successful outcome in a case of mesenteric thrombosis diagnosed on the basis of classical signs and symptoms. In addition, it is believed that awareness of the newer concepts in fluid balance proved an invaluable adjunct in the favorable management of the patient's condition.

A seventy-six year old white male was admitted to the medical service of the New York Polyclinic Hospital on November 14, 1949, with the chief complaint of malaise of one week's duration. About seven days prior to admission, he began to complain of anorexia, nausea, vague generalized upper abdominal and lower back pain.

The day prior to admission, he vomited for the first time some black-looking material and at the same time continued to feel progressively weaker, experiencing an aggravation of the symptoms already described.

There was no history of chills or fever, no known food intolerance or postprandial distress. There had been no change in bowel habits nor diarrhea, tarry stools or weight loss.

Systemic Review:—Essentially noncontributory except for frequency of urination with slowing of urinary stream for the past eight years.

Past History:—Except for removal of a superficial tumor from his back two years ago at this hospital, there were no other operations or serious illnesses.

Family History and Occupational and Social History:—Noncontributory.

Physical Examination:—On admission revealed a well-developed and well-nourished male in no acute distress with a blood pressure of 150/86, pulse 100, full and regular and a rectal temperature of 98°F. Examination of head, skin, ears, eyes, nose, throat, neck, lungs, cardiovascular system and extremities revealed no abnormal findings. The abdomen was obese and symmetrical, showing slight dilatation and voluntary muscle spasm throughout, although no real tenderness or

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rebound tenderness could be elicited. Liver, kidneys and spleen were not palpable. No masses or fluid could be palpated. Tympany over left upper quadrant on percussion. On auscultation, no borborygmi but occasional tinkles were heard.

Rectal examination revealed good sphincter tone, firm, one plus uniform enlargement of the prostate, no abnormal masses in the rectum and normal consistency and color of stool on glove.

Laboratory Studies on Admission:—White blood cells 29,000, Poly. 93 per cent, Leucocytes 6 per cent, monocytes 1 per cent. Red blood cells 4,720,000, hemoglobin 92 per cent. Blood sugar 141 mg., Blood urea nitrogen 42.5 mg., Creatinin 1.2 mg., Urinalysis:—Specific gravity 1.022; 3 plus albumin; sugar negative. Many coarse and innumerable fine granular casts.

The day following admission, November 15, the patient was still vomiting and became comatose in spite of supportive and symptomatic therapy.

On the second day after admission, November 16, a gastric drainage specimen was markedly positive for occult blood. A Miller-Abbott tube was inserted and suction instituted.

Roentgenography:—Flat plate of the chest and abdomen showed lungs to be clear, heart enlarged with prominence of the left ventricle and diaphragm to be slightly elevated bilaterally. There was marked dilatation of the loops of the proximal small intestine chiefly on the left side of the abdomen.

Barium enema was done and the barium flowed readily, outlining the entire colon without evidence of obstruction or deformity. There were multiple fluid levels seen in the dilated small intestine.

These findings were consistent with high small intestinal obstruction at about the level of the mid-distal jejunum.

Surgical consultation corroborated the clinical findings. Patient was comatose and responded to painful stimuli; the abdomen was soft with some voluntary spasm, on deep pressure the patient moaned. There was tympany in the left upper quadrant of the abdomen which was still silent on auscultation.

After a four-hour wait, a repetition of the scout film of the abdomen revealed the same small intestinal loops to be as dilated as before with no progression of the gas column. The patient was still comatose and his blood pressure had dropped from 150/86 to 120/80. It was concluded that the patient had a mechanical obstruction due to a congenital band, internal hernia or mesenteric thrombosis.

Following an electrocardiographic examination which showed essentially normal findings, an exploratory laparotomy was performed by one of us (L.M.R.) under local anesthesia. A right paraumbilical incision was made and the abdominal cavity entered. Considerable free bloody fluid was encountered and a loop of midjejunum was found to be dusky-red in color and markedly indurated. The mesentery supporting this portion of the jejunum was likewise thickened and discolored. This loop was found to have been rotated about 180° on the mesenteric axis. This rotation was corrected and after observing the bowel for fifteen minutes, to allow return of circulation, sixteen inches of jejunum which did not improve,

were resected and an end-to-end anastomosis performed. During the operation, the patient received continuous oxygen, small amounts of sodium pentothal and 500 c.c. of blood. Patient left operating room in good condition. Later pathological report confirmed operating room diagnosis of mesenteric thrombosis with early gangrene of bowel.

Postoperatively, the patient was placed on anticoagulant therapy (depo-heparin 300 mg. I.M. one dose) followed by oral danilone (50 mg. first day and 50 mg. a day p.r.n. to maintain a prothrombin time of 30-40 sec.), streptomycin (0.25 gm. q.i.d.) and penicillin (100,000 units) every three hours, Levine tube suction drainage and amino acid solution. However, in spite of the electrolytic balance as evidenced by normal blood chemical findings (blood urea nitrogen 27.5, chlorides 440, carbon dioxide combining power 56), the patient continued in a state of semi-coma on the second postoperative day.

It was then decided, following a repetition of the electrocardiogram with normal findings, that potassium chloride therapy through the Levine tube might be indicated strictly on an empirical basis. Eight grams of this substance in four divided doses were given through the Levine tube in twenty-four hours. Definite improvement in the patient's clinical status was in evidence twelve hours following the administration of potassium chloride; he regained consciousness and his temperature returned to a normal level. Potassium chloride therapy in lower doses, 4 gm. the second day and 2 gm. a day in subsequent days, was continued for three more days.

His recovery, thereafter, was uneventful. He remained in the hospital for twenty days following the operation and was then followed in Surgical Clinic with no further untoward symptoms referable to the gastrointestinal tract.

Conclusions:—1. A clinical picture of *silent* abdomen, occult blood in stomach contents, x-ray evidence of small intestinal obstruction without a history of previous abdominal surgery or presence of an external hernia should be strongly indicative of mesenteric thrombosis.

2. Local anesthesia with continuous oxygen and slight amounts of sodium pentothal have their rightful place in the management of such poor-risk patients.

3. Attention to careful postoperative electrolytic balance with the possible influence of potassium depletion should be of paramount importance in cases of this or similar nature.

REFERENCE

Johnson, C. Clifford and Baggenstoss, Archie H.: Proc. Staff Meet. Mayo Clin. **24**:633, (Dec. 7), 1949.

GASTROILEOSTOMY FOLLOWING SUBTOTAL GASTRECTOMY

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Massive resections of small intestines have been performed by many surgeons in the past. These were necessary because of pathologic involvements such as extensive ileitis, malignant lesions, gangrene, etc. Haymond[1] in a review of 257 such resections found a mortality rate of about 33 per cent. It was established from this study that a patient can withstand resections of up to 50 per cent of the small intestines with the remainder of the digestive tract still carrying on normal function.

Diarrhea was noted as the most common postoperative complaint. This type of diarrhea could not be controlled by drugs, but relieved by proper dietary management, such as adequate carbohydrates and proteins with low fats. There are several cases on record where only three feet of small intestines were left; these patients developed tetany in addition to the above symptoms.

A rare surgical error, when a patient is operated upon for peptic ulcer, is the faulty anastomosis of ileum to stomach, forming a gastroileostomy instead of a gastrojejunostomy. Twenty-six such cases have been reported in the literature since 1915.

Martin and Carroll[2] in 1915 reported the first case of gastroileostomy in a young woman. The error was first recognized two years after the initial operation for the relief of ulcer symptoms. The gastroileostomy was about twenty inches from the ileocecal valve. Mercur[3] in 1917 reported the second case in a 30 year old female where the gastroileostomy was first noted three years after the original operation for ulcer. The anastomosis was about six inches from the ileocecal valve. He also cited a case operated upon by Judd in 1912 where the anastomosis was within five inches of the ileocecal valve. This patient died from starvation acidosis. Rivers and Wilbur[4] in 1932 reported nine cases, eight of which were proven at operation and one was noted after x-ray studies. Kogut and Stein[5] reported three cases, two of which were recognized at operation and one at autopsy. Smith and Rivers[6] in 1943 reported eight additional cases, all proven at operation. Brown, Colvert and Brush[7] in 1947 reported three cases and evaluated the symptoms in all reported cases. They noted that weight loss was prominent in nineteen cases, pain in seventeen, diarrhea in fourteen, vomiting in six, ileac ulcers in six and hemorrhage in three cases.

Symptoms frequently occurred immediately after operations in many of these patients. In other cases, the symptoms appeared rather late. In those in whom the symptoms appeared late, food was probably leaving the stomach, mostly through the patent pylorus, rather than the gastroileostomy. In only seven of the reported cases was the diagnosis made by x-ray findings. Refilling of the stomach with

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barium through the gastroileostomy after the stomach had emptied was noted in two cases by Brown, et al.

The case presented here is rather unusual because it is the first known case of gastroileostomy following subtotal gastrectomy for a perforated peptic ulcer. The gastric stoma was anastomosed to the terminal ileum about six inches from the ileocecal valve. All of the twenty-one feet of the small intestines have been excluded. Food ingested, entered immediately into the colon. Exclusion of the bile, pancreatic and intestinal enzymes and the entire small intestinal tract resulted in a rapid deterioration in the health of this patient.

Case Report

The patient, a 50 year old male, an upholsterer by occupation, came to our attention on January 19, 1950, with a history of a known peptic ulcer syndrome

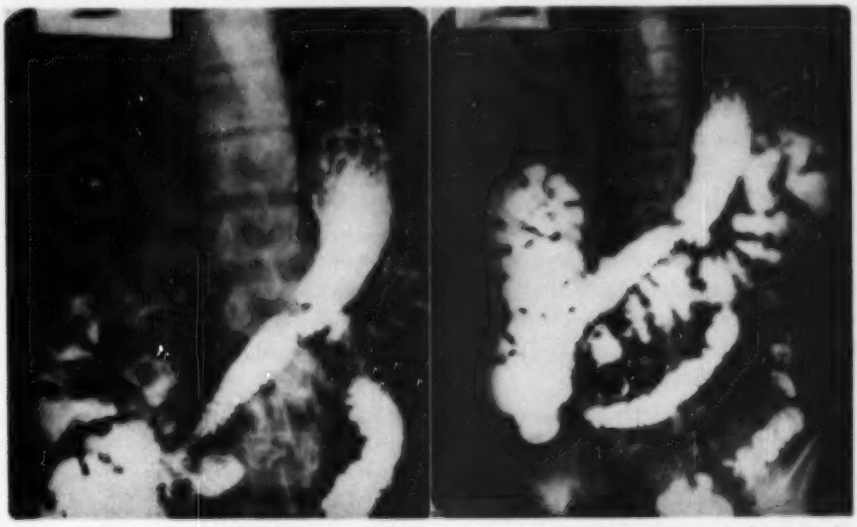

Fig. 1—Immediate plate after ingestion of the barium meal. The gastroileostomy can be seen, the ileum is noted connecting with the cecum.

Fig. 2—The entire colon visualized about ten minutes after ingestion of the barium meal.

since 1930. During this period, he had the usual pain relieved by food recurring an hour or two after meals, frequent night distress and periods of remission. He had been x-rayed a number of times and the diagnosis of duodenal ulcer was corroborated. His brother, also an upholsterer, had a similar digestive disturbance and a diagnosis of duodenal ulcer was made. In May, 1949, his brother developed intractable pain and a gastrectomy was performed for a penetrating ulcer, with good recovery. Soon after this episode, the patient's pain became aggravated. On October 26, 1949, he was re-x-rayed and during this study he developed excruciating pain, apparently an impending perforation. He was hospitalized immediately, and on October 30, 1949, he was operated upon for a perforated ulcer. A subtotal gastrec-

tomy was performed. The postoperative course was rather stormy; he developed a postoperative pneumonia and a renal shutdown with a high azotemia. The patient states that except for the relief of pain, he has not been well since the operation. He had constant anorexia, nausea, weight loss, tenesmus and diarrhea immediately after eating. He also complained of symptoms suggestive of the dumping syndrome. The stool was light in color and soapy. About five to six weeks after the operation, he began to vomit daily. He became weaker and lost about 30 pounds since the operation. He was re-x-rayed by his physician and was assured that he was doing well.

On January 19, 1950, about three months after the operation, when he came to our attention, his chief complaints were weakness, anorexia, weight loss, nausea, vomiting, diarrhea with soap-like stool and swelling of the lower extremities. The physical examination revealed an anemic emaciated male, about fifty years of age, his weight was 111 pounds (the weight before the operation was 142 pounds), the remainder of the physical examination was noncontributory except for the edema of the lower extremities which suggested a hypoproteinemia.

Fluoroscopic and x-ray examintion after a barium meal revealed a subtotal gastrectomy. The barium emptying immediately into the colon. X-ray plates taken immediately after ingestion of the meal showed it to be in the rectal ampulla, and except for a few inches of the terminal ileum, no other small intestines were identified.

A diagnosis of gastroileostomy, with exclusion of the small intestines, was made. The patient was advised to submit to surgery for the revision of the gastroileostomy and reestablishment of the gastrojejunostomy. He was admitted to the Brooklyn Jewish Hospital on January 26, 1950, where laboratory studies before the operation revealed the following:

Blood Count—Hgb., 65 per cent; R.B.C., 3,300,000; W.B.C., 5,550; Polys, 62 per cent; Lymph., 33 per cent; Baso., 2 per cent; Mono., 3 per cent.

Sed. Rate—2 mm.; Stool—Positive for blood, negative for bile.

Chemistries—Blood sugar, 120 mg. per cent; Urea, 14 mg. per cent; Total protein, 4.7 mg. per cent; Albumin, 2.5 mg. per cent; Globulin, 2.1 mg. per cent; A/G Ratio, 1.1; Calcium, 9.5 mg. per cent; Phosphorus, 2.6; Potassium, 17.7; Phosphatase, 4.8; Chlorides, 361 mg. per cent; Ceph. Floc., plus 4; Icterus Index, 8.4; Thymol turbidity, 5.9; CO_2 combining power, 68.4 volume per cent.

Mazzini test, Negative. Prothrombin Time, 11, against control of 11. Gastric Contents examined revealed no free HCl and total acidity of 4.8 units.

After the above laboratory data were obtained, the patient was prepared for surgery by blood transfusions, daily intravenous infusions of Amigen, glucose and saline and Vitamin B and C.

On February 3, 1950, the patient was operated upon under endotracheal inhalation anesthesia. Upon opening the abdominal cavity, numerous adhesions were encountered and when liberated the gastroileostomy was isolated. The stoma was noted to be about five inches from the ileocecal valve. After the anatomy was def-

initely identified, the gastroileostomy was revised by severing the stomach just proximal to the stoma. The distal edge of the gastric wall about ½ cm. in width was inverted, thus reestablishing the continuity of the ileum. The proximal portion of the remnant stomach was properly anastomosed to the first portion of the jejunum, just beyond the ligament of Treitz. The postoperative course of the patient was entirely uneventful, patient noticing a feeling of well-being from the first postoperative day. The wound healed by primary union and he was discharged on February 12, 1950, the ninth postoperative day. He tolerated well a rather full postgastrectomy diet as prescribed for the ambulant patients upon discharge from the hospital.

Summary

This case is presented because of its rarity, being the 27th case of gastroileostomy. It is the first known case in which a gastrectomized stump was sutured to the ileum, thus completely excluding the entire small bowel segment with all its enzymatic actions. This factor was responsible for the patient's inanition and practical starvation, with its accompanying loss of protein and fat in the stool producing a sprue-like syndrome.

In this patient, unlike the other twenty-six cases cited in the literature, the symptoms appeared immediately after the operation because the food entered through the only channel, gastroileostomy into the colon, whereas in the other cases, some of the food entered into the jejunum through a patent pylorus.

References

1. Haymond, H. E.: Surg. Gynec. & Obst. **61**:693, 1935.
2. Martin, F. and Carroll, A. H.: Ann. Surg. **61**:567, 1915.
3. Mercur, W. H.: Tr. Am. Climat. & Clin. Assoc. **33**:122, 1917.
4. Rivers, A. B. and Wilbur, D. L.: Surg. Gynec. & Obst. **54**:937, 1932.
5. Kogut, B. and Stein, E.: Am. J. Surg. **33**:263, 1936.
6. Smith, L. A. and Rivers, A. B.: Surg. Gynec. & Obst. **76**:110, 1943.
7. Brown, C. H., Colvert, J. R. and Brush, R. E.: Gastroenterology. **8**:71, 1947.

ESOPHAGEAL DYSPHAGIA, ASSOCIATED WITH GALLBLADDER DISEASE

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It has been a matter of general knowledge that reflex esophageal dysphagia may be associated with various disorders of the gastrointestinal tract. Although this condition is mentioned in the literature and textbooks, only meager consideration is given to this subject. Actual roentgenologic portrayal of the spastic phenomena of the esophagus has infrequently been shown. As far as can be ascertained, there have been few illustrative cases recorded which demonstrate spastic obstruction of the esophagus secondary to gallbladder disease.

This subject is therefore of sufficient interest to warrant a brief communication. The purpose of this presentation is to report two illustrative cases, one of spasm, the other of stricture and spasm associated with gallbladder disease. Reflex spasm of the esophagus secondary to gallbladder pathology is not infrequently encountered in the routine gastrointestinal roentgen study. There seems to be well grounded physiologic evidence that gastrointestinal and gallbladder affections may be an inciting factor in the production of secondary reflex spasm of the esophagus. The cardia is usually involved in most cases of reflex esophageal spasm, though the upper and midesophagus may also be affected. True cardiospasm, or achalasia of the esophagus, is not to be confused with reflex spasm and is not considered here.

Clinically, spastic phenomena of the esophagus usually presents symptoms of a mild nature, and rarely produces obstructive signs. The usual symptoms encountered in esophageal reflex spasm are substernal distress, nausea, heartburn, regurgitation, and occasionally vomiting. Rarely, are there any signs of esophageal obstruction. The esophageal symptoms are brought about regardless of the consistency of the substance swallowed. The swallowing of fluids may bring on the symptoms just as well as solids. In most instances, there is greater distress on swallowing solids because of the marked contracture induced by the solid bolus. This phenomenon is well illustrated in one of our cases, when the bariumized pledget of cotton was delayed for long periods at two points within the esophagus. This phenomenon was not as clearly shown while swallowing the liquid barium. In reflex spasm the esophageal symptoms are not usually severe enough to warrant an esophagoscopic examination. In fact, esophagoscopy is rarely performed in these cases, because the symptoms are most often transitory. Persistent vomiting, as a result of esophageal obstruction is a very rare finding in reflex spastic conditions of the esophagus, and when it is encountered, it is more apt to be due to an organic lesion, rather than simple esophageal spasm. In spite of the fact that reflex esophageal dysphagias are commonly observed clinically, such cases are not often recognized during the roentgenologic examination. This is due to several factors. First, in the routine roentgen examination, a liquid barium meal is swallowed in the erect position; this liquid

meal usually passes down the esophagus rapidly and little attention is given to slight delays in its descent. Secondly, unless otherwise indicated, a solid opaque bolus is rarely given in the routine examination. The esophagus, therefore, is not examined in great detail, and thus, the simple spastic phenomena are not too often demonstrated. It is only when there is a marked delay in the descent of the opaque meal, that our attention is focused on a localized area of the esophagus and then the

Fig. 1—Case I. a) A bariumized pledget of cotton is shown in the midesophagus, remained stationary at that site for over 30 minutes.

b) Roentgenogram made about 40 minutes after swallowing the bariumized pledget of cotton, showing its descent from the midesophagus to the cardia end, where it remained for a long period before entering the stomach. The cardia end is bulbus and slightly dilated.

possibility of an esophageal lesion or a spastic phenomenon is considered. These factors probably account for the paucity of information concerning reflex spasm of the esophagus. In every case of esophageal dysphagia, a thorough and carefully planned study of the esophagus should be made to eliminate the possibility of an organic lesion. The roentgen method of examination stands preeminently as the procedure of choice in the routine examination of the esophagus. Spastic phenomena may also be observed esophagoscopically.

The following two cases are presented to illustrate the roentgen picture of esophageal reflex spasm and stricture, encountered secondary to and/or associated with gallbladder disease.

Case 1:—Female, aged 49, complained of difficulty in swallowing for nine months. The dysphagia was more pronounced upon swallowing solid foods, but even liquids at times caused esophageal symptoms. The patient was well developed. There was no loss of weight. Her esophageal symptoms were intermittent, with periods of relief of varying intervals. She has had attacks of upper abdominal pain and other gastrointestinal symptoms referable to the gallbladder. A year prior to

Fig. 2—Case 2. Illustrates a stricture with associated spasm of the lower end of the esophagus shown at arrows. It produced intermittent signs of esophageal obstruction.

the onset of the esophageal dysphagia, a gallbladder examination revealed the presence of gallstones. Because of the persistence of her esophageal symptoms a gastrointestinal roentgen study was undertaken. This examination revealed a spastic contracture in the midesophagus and also at the cardia end. Upon swallowing a large pledget of cotton impregnated with barium, the pledget became wedged in the midesophagus and remained there for over 30 minutes. It later reached the cardia end where its passage was again delayed for a long period before entering the stomach. The cardia end of the esophagus was bulbus and slightly dilated. These examinations were repeated, and at each time a similar picture was obtained. An esophagoscopic examination revealed no intrinsic pathology. The esophageal symptoms

disappeared following the esophagoscopic examination. A roentgen re-examination of the esophagus, several weeks after the esophagoscopic examination, likewise showed a disappearance of the spastic phenomenon. Since then, however, the symptoms of esophageal distress have recurred at various intervals. It was obviously concluded that the dysphagia was due to a reflex spasm secondary to the gallbladder condition.

Case 2:—Male, aged 50. The patient complained of intermittent periods of dysphagia for a period of four years. The difficulty in swallowing was encountered in periodic spells, and then, only when he swallowed meats and heavy solids. However, there were intervals when he had no esophageal symptoms. He also complained of frequent regurgitation of food and vomiting after eating, with epigastric pain and upper abdominal discomfort. He was an alcoholic and had lost considerable weight. Physical examination revealed nothing of interest. An x-ray examination of the gallbladder revealed a faint shadow of the gallbladder, with poor dye concentration and a failure of the gallbladder to contract following a fat meal, which suggested evidence of a cholecystitis. There were no radiable stone shadows but on account of the faintness of the gallbladder shadow, stones could not be eliminated. Roentgen examination of the gastrointestinal tract showed evidence of an esophageal spasm and stricture at the cardia end. The stricture was smooth in contour and appeared to be of benign nature. Esophagoscopic examination revealed the stricture as depicted in the roentgen examination, but no other demonstrable intrinsic pathology could be seen. There was no relief of the esophageal symptoms immediately following dilatation of the stricture. The patient claimed that the dilatation increased his symptoms and caused him considerable pain, which he did not have before. For the next six months the patient remained asymptomatic and was able to swallow solids, but he had intervals when the dysphagic signs would return in a mild form. Some months later he suddenly had an acute catastrophe, with abdominal pain, which required an emergency operation, at which time an acute gallbladder with gallstones was found. After the operation the patient's esophageal symptoms subsided dramatically. Because of the complete disappearance of esophageal symptoms, the patient refused to be re-x-rayed. This case presented a stricture and spasm at the cardia end of the esophagus associated with gallbladder disease.

Summary

Two cases, one of reflex esophageal spasm, the other a stricture with associated spasm of the esophagus are presented to illustrate the secondary effect or association of esophageal dysphagia with gallbladder disease. Intermittent esophageal obstructive signs secondary to gallbladder disease is uncommon. The demonstration of spastic phenomena by indisputable roentgenologic evidence has been infrequently recorded. The use of large pledgets of barium impregnated cotton is of invaluable aid in the roentgen study of the esophagus. The two cases are fully described, both of which presented a history of intermittent esophageal obstruction and upper abdominal symptoms, due to gallbladder pathology.

HEMOCHROMATOSIS*

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Hemochromatosis is classically described as a rare and fatal disease due to a disturbance in iron metabolism, characterized by the deposition of hemosiderin and hemofuscin in the skin and viscera, and manifested clinically by bronze pigmentation of the skin, enlargement of the liver and diabetes mellitus. Recent clinical and experimental investigations tend to cast doubt upon the rarity and pathogenesis of this disease. Although the triad of symptoms mentioned above may be present in a large percentage of far advanced cases, it is conceivable that in the early evolution of the disease none of these symptoms may be present. In other cases, as exemplified by one of our patients, hepatomegaly may be the only presenting sign. The advent of needle liver biopsy has made possible earlier recognition of the disease in such instances. Evidence of hypogonadism, so frequently found in patients with this disease, may be more easily ascertained by hormonal assays which the modern endocrine laboratory can perform. The formerly grave prognosis has been altered in recent years by the improved methods of treating the serious complications of the disease so that the duration of life may be expected to expand parallel with the advances in the therapy of diabetes, portal cirrhosis, pneumonia and tuberculosis. It is the object of this paper to review the recent literature pertaining to hemochromatosis and present two patients who did not show all of the classical symptoms but in whom a definite diagnosis was established.

Case Reports

Case 1:—No. 193027, L.G., a 38 year old white male, Jewish butcher, was admitted to Beth El Hospital on February 3, 1949 with a vague history of multiple pains of 2 years duration. At the onset he complained of pain in the left upper chest, unrelated to effort, nonradiating and unassociated with any other cardiorespiratory symptoms. A few months before admission the patient developed a sticking pain in the right upper abdomen, unrelated to meals or respiration, and not associated with any gastrointestinal symptoms. A few weeks before admission pain was experienced in the mid-back over the region of the eleventh thoracic vertebra. All of these pains were present upon admission. He stated that his genitals were small and his sexual desires diminished.

Physical examination revealed a short, well developed male, in no acute distress. The skin and mucous membranes were not pigmented and the sclerae were not jaundiced. The axillary and chest hair were sparse and the pubic hair showed a

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female type of distribution. The heart and lungs were normal. The blood pressure was 130/80. The liver and spleen were both felt 2 fingers below the costal margins. The external genitalia were slightly smaller than normal. There was no gynecomastia.

Laboratory data:—The urine was negative. The blood count was normal. Blood chemistries disclosed a fasting blood sugar of 86 mg. per cent, urea nitrogen of 15 mg. per cent, calcium of 9 mg. per cent, phosphorus of 5.6 mg. per cent, alkaline phosphatase of 1.4 Bodansky units, cholesterol of 140 mg. per cent, cholesterol esters of 125 mg. per cent, and a total serum protein of 6.3 gm. per cent with an A/G ratio of 4.6/1.7. Liver function tests showed a bromsulfalein retention of less

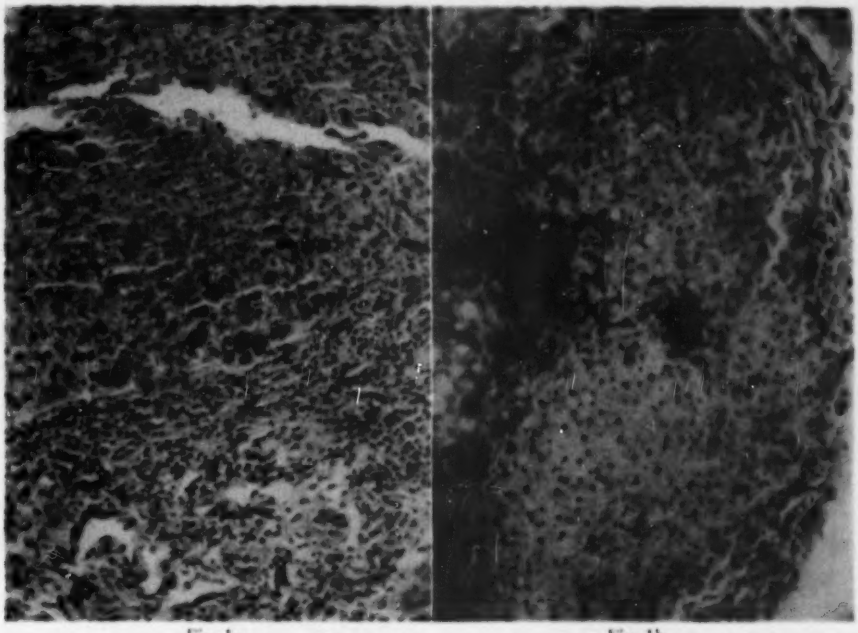

Fig. 1a Fig. 1b

Fig. 1—a) Hemosiderin in liver cells (hematoxylineosin stain).
b) Case I. Hemosiderin in liver cells (iron stain).

than 5 per cent in 45 minutes, a zinc turbidity of 5.5 units, a cephalin flocculation of 3 plus in 24 hours, a hippuric acid excretion of 1.5 grams after oral administration of sodium benzoate, and a prothrombin activity which was 47 per cent of normal. The glucose tolerance test showed a tendency toward a diabetic type of response. The fasting blood sugar was 94 mg. per cent, and 4 hourly blood specimens after ingestion of 100 grams of glucose showed values of 125 mg. per cent, 222 mg. per cent, 117 mg. per cent and 83 mg. per cent. Bone marrow aspiration was normal. X-ray studies of the gastrointestinal tract, gallbladder, spine, ribs and long bones were negative.

Hormonal assay of the urine showed a total neutral 17 ketosteroid excretion of 12.4 mg. and 12.9 mg. in 24 hours on 2 occasions. Assay of the urinary gonadotropins (FSH) showed a negative reaction at the level of 80 mouse units per liter. Less than 4 rat units of estrogen (in terms of estrone) were excreted in 24 hours.

Skin biopsy was negative. Liver biopsy obtained with the Vim-Silverman needle showed definite evidence of portal cirrhosis with extensive hemosiderosis (Fig. 1).

The patient was placed on a high caloric, high vitamin, high carbohydrate, high protein and moderate fat diet and told to abstain from alcohol. He was discharged February 19, 1949. At a recent visit to our follow-up clinic he stated that he was working and enjoying fairly good health. The physical findings were unchanged.

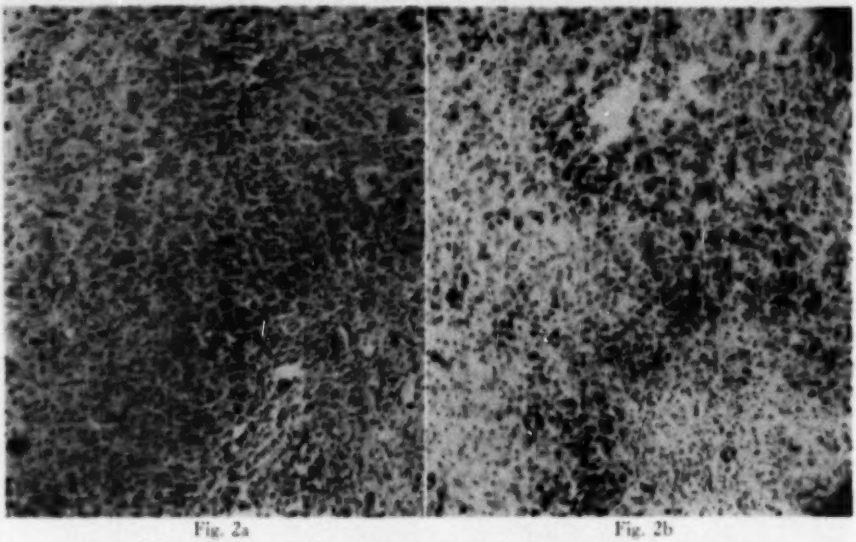

Fig. 2a Fig. 2b

Fig. 2—a) Case 2. Hemosiderin in liver cells (hematoxylin-eosin stain).
b) Case 2. Hemosiderin in liver cells (iron stain).

Case 2:—No. 193377, H. H., a 50 year old white male, sales supervisor, was admitted to Beth El Hospital on January 15, 1949 because of tarry stools and hematemesis. In 1930 he developed polydypsia, polyuria and lost weight. Glycosuria and hyperglycemia were found. He was given a diet and 30 units of protamine zinc insulin once daily. His diabetes steadily became more difficult to control so that by 1946 he stated that he was taking 150 units of protamine zinc insulin once daily. At the time of admission he was taking 100 units daily. Since 1926 the patient was a severe alcoholic. From 1946 until one month before admission he drank one pint of whisky daily. Notwithstanding this the patient stated that his dietary intake of proteins, fresh fruits and vegetables was always adequate. About 10 years before admission his physician noted an enlarged liver. In December, 1948 the patient complained of enlargement of the abdomen, generalized abdominal pains, postpran-

dial nausea, anorexia and loss of libido. X-rays of the stomach at that time were normal. A gallbladder series revealed cholelithiasis. An enlarged liver was noted. His physician prescribed a high protein, high vitamin, low fat diet. On January 14, 1949 the patient had a copious tarry stool. On January 15th he suffered a massive hematemesis, intense melena and symptoms of collapse, following which he was admitted to the hospital.

Physical examination disclosed a tall, thin adult male, acutely ill, with a rapid pulse and pallor of the face. The skin of the exposed portions of the body appeared irregularly bronzed. The patient ascribed this to a sun tan. There was no increase in pigmentation of the nipples, genitalia, anus or body creases. There was no mucosal pigmentation. The sclerae were not icteric. A few spider telangiectases were noted on the chest and neck. The heart and lungs were normal. The blood pressure was 100/70. The liver was enlarged to the umbilicus in the midclavicular line, slightly tender, smooth and firm. The edge of the left lobe was felt 2 fingers below the left costal margin in the epigastrium and left upper quadrant. The spleen was palpable 4 fingers below the costal margin in the extreme left flank, lateral and superficial to the enlarged left lobe of the liver. There was no shifting dullness or fluid wave. The external genitalia appeared normal. There were no hemorrhoids. There was slight pitting edema of both ankles. Axillary and chest hair was sparse, and the pubic hair of female distribution. There was no gynecomastia.

Laboratory data:—Upon admission he had a hemoglobin of 68 per cent, a white cell count of 14,000 with 75 per cent polymorphonuclear cells. The urine showed 4 plus sugar and acetone. The fasting blood sugar was 420 mg. per cent and the CO_2 combining power 36 vol. per cent.

Course:—After blood transfusions, parenteral fluids and insulin, the patient made a rapid recovery. All signs of gross bleeding disappeared.

Studies of liver function revealed a total serum protein of 7.9 gm. per cent with an A/G ratio of 4.3/3.6. The quantitative Van den Bergh was 0.2 to 0.5 mg. per cent. The zinc turbidity tests varied from 11 to 12.5 units but later rose to 35 units. The bromsulfalein test showed a retention of less than 5 per cent of the dye in 45 minutes. The total cholesterol was 200 mg. per cent and the cholesterol esters were only 45 per cent of the total. Cephalin flocculation was at first 1 plus in 18 hours and on subsequent examinations was 3 and 4 plus. The prothrombin activity, which at first was 56 per cent of normal, subsequently became 100 per cent. Repetition of all other function tests showed essentially the same findings as those previously noted. The Robinson-Power-Kepler test was equivocal. A gastrointestinal x-ray series showed the presence of esophageal varices. A gallbladder x-ray series showed the presence of cholelithiasis. The patient was discharged markedly improved on Feb. 3, 1949 with instructions as to dietary care and on an insulin mixture consisting of 68 units of regular insulin and 34 units of protamine zinc insulin.

He was readmitted 17 days later on Feb. 20, 1949 because of massive hematemesis and melena of a few hours duration. The physical examination was as pre-

viously noted with the addition of shifting dullness and a fluid wave in the abdomen. He responded immediately to the same measures as on his original admission.

Liver function tests were essentially the same as previously noted. In addition, a hippuric acid test showed an excretion of 1.1 gm. after oral administration of sodium benzoate.

Hormonal assay of the urine showed a total neutral 17 ketosteroid excretion of 5.9 mg., 7.0 mg. and 8.5 mg. on 3 different occasions. Fractionation of the total on the second test showed an alpha fraction of 72.9 per cent and a beta fraction of 27.1 per cent. Assay of the urinary gonadotropin (FSH) showed a doubtful reaction at the level of 80 mouse units per liter. Less than 4 rat units of estrogen (in terms of estrone) were excreted in 24 hours.

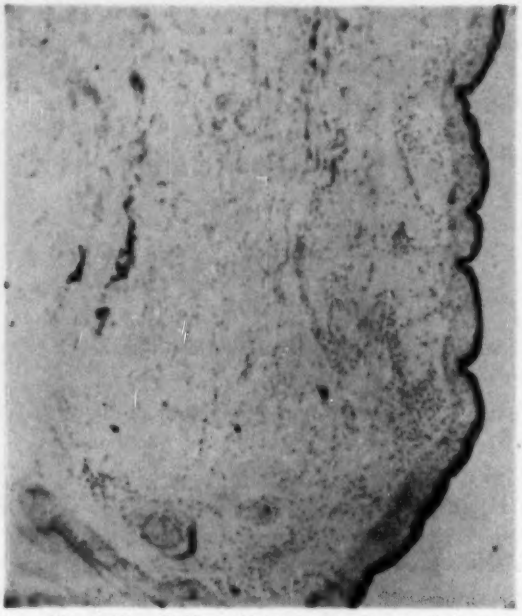

Fig. 3—Case 2. Hemosiderin in skin (iron stain).

Liver biopsy obtained with the Vim-Silverman needle showed definite evidence of pigment cirrhosis (Fig. 2). Skin biopsy showed focal iron pigment accumulations (Fig. 3).

The patient was readmitted for the third time on April 22, 1949 for operative intervention as a means of preventing subsequent, and perhaps fatal, esophageal hemorrhage. He was comfortable and had no evidence of bleeding since his discharge. Gauze packing and talcum powdering of the posterior mediastinum was carried out by Dr. Neuhof on April 26, 1949. It was hoped that by this procedure new vessels would be formed in the granulation tissue which, by diverting blood from the esophageal veins, would decrease the pressure within these vessels and

thus prevent serious hemorrhage. Aside from the complication of a small post-operative empyema the patient made an uneventful recovery. He was discharged from the hospital on June 11, 1949 clinically much improved.

Follow-up disclosed that the patient was admitted to another hospital on Aug. 13, 1949 because of a tarry stool. There was no hematemesis. He received a transfusion of 500 c.c. of whole blood and was discharged on Aug. 24, 1949.

Discussion

Incidence:—In 1935 Sheldon[1] was able to collect only 335 cases of hemochromatosis in an exhaustive review of the world literature. By 1942 Humphrey, et al[2] found 400 acceptable cases in the literature. The rarity of the diagnosis may be appreciated by noting the findings at some of the larger North American clinics. McPhedran[3] reports 9 cases found in 13 years at Toronto Hospital where some 4,300 patients are seen annually. Butt[4] reports 30 cases seen at the Mayo Clinic from among approximately one million admissions. John[5] found one case among 4,491 diabetics and at the Joslin clinic[6] 24 cases were collected from the records of 21,500 diabetics. Strachan[7] on the other hand found 33 cases in 1,100 autopsies at the Johannesburg Hospital, an incidence of 3 per cent. Gillman[8] found 15 cases of pigment cirrhosis in liver biopsies performed upon 120 pellagrins at the same hospital. Adding 15 with precirrhotic livers and excluding patients under 10 years of age, he estimated a 30 per cent incidence of hemochromatosis in pellagrins. Herbut and Tamaki[9] found 12 cases of diabetes mellitus among 115 necropsied cases of cirrhosis of the liver. Fifty-one of 60 cases, in which histologic sections of the pancreas were available for re-examination, disclosed diffuse fibrosis of the pancreas.

Pathology and pathogenesis:—Sheldon[1] has excellently described the pathologic anatomy of hemochromatosis in great detail. It need only be stated here that the organs of predilection are the liver, pancreas, spleen and kidney. The gastrointestinal tract, cardiovascular and respiratory systems are also frequently involved. The pigment has been studied in great detail and several features are noteworthy. There are 2 pigments, the iron-containing hemosiderin, and the non-iron-containing hemofuscin. Hemosiderin is found in the liver cells chiefly at the periphery of the lobule, in fibrous tissue (chiefly extracellular), in the Kupfer cells, infrequently in the vascular endothelium, and in great concentrations in the pseudo-bile canaliculi. Hemofuscin is distributed mainly in the connective tissue cells of the adventitia of large vessels, in the smooth muscle cells of the media of large vessels, in the connective tissue and rarely in the liver cells.

The observations of Gillman, et al[8] are of extreme interest. He found, among 120 South African natives admitted for pellagra, that the presence of a fatty liver was as constant a feature as rash and edema. Pigmentation of the liver cells with hemosiderin and hemofuscin, in addition to fatty changes, was found in a number of the cases. Pigmentation of reticuloendothelial cells as well as of parenchymatous cells with clumps of pigment in the portal tracts was found in another group of

cases. Pigment cirrhosis with intense fibrosis was found in 15 cases. By histochemical studies the authors demonstrated that hemosiderin is derived from mitochondrial elements. Thus we appear to have histologic evidence of the pathological evolution of pigment cirrhosis indistinguishable from that found in classical hemochromatosis at autopsy.

In the study by Herbut and Tamaki[9] previously mentioned, detailed examination of their 51 cases for cirrhosis and pigmentation of the liver, and fibrosis and pigmentation of the pancreas, with and without diabetes, showed that there were 6 definite combinations with subtle transitions from one group to another. They concluded that there is a definite relation between simple cirrhosis of the liver, diabetes and hemochromatosis. In cases of hemochromatosis it was their opinion that cirrhosis of the liver and diabetes may be caused by a single substance, a ureide, and that the cirrhosis may further be aggravated by dietary deficiencies and hypercholesterolemia. Fibrosis of the pancreas results from portal hypertension, consequent to hepatic cirrhosis, and hemosiderosis follows an abnormal retention of iron derived exogenously, and perhaps to some extent endogenously. In confirmation of these deductions Herbut, et al[10] found that 10 of 30 rabbits injected with alloxan developed severe periportal necrosis of the liver. Two others developed diabetes and portal cirrhosis and showed minimal depositions of iron in the liver, spleen and pancreas. One of the latter animals also disclosed interlobular and intralobular fibrosis of the pancreas. Reduced iron fed freely to the diabetic rabbits for only two and one-half weeks caused a marked deposition of the pigment in the spleen, intestinal mucosa, liver and renal tubules.

The theories of toxins (copper, iron, bacteria, alcohol), hemolysis, and disordered iron metabolism in the pathogenesis of hemochromatosis are unconvincing. Gillman, et al[8] presented the first substantial evidence to account for the picture of hemochromatosis. The concept of a nutritional deficiency is consonant with recent studies of the etiology of portal cirrhosis. The studies of Herbut and his associates[9,10] supplement those of Gillman. The evidence thus accumulated points to a deficiency disease which in some manner upsets the intracellular iron physiology which sets the picture of hemochromatosis in motion. Our Case 2 fits well into this concept. With study of intracellular chemistry we may expect further elucidation of this fascinating problem which will enable us to discard the verbiage of inborn error of metabolism and hemochromatosis for more accurate and definitive terminology.

Clinical course:—The disease has not been described in anyone under the age of 20. Over 95 per cent of the cases have been found in males, only 13 cases having been reported in females. Twenty per cent of the men and 30 per cent of the women gave histories of alcoholism. Diabetes was the initial complaint in 25 per cent, upper abdominal pain or hepatomegaly in 25 per cent, and pigmentation of the skin in 25 per cent. About 10 per cent complained only of weakness. Miscellaneous complaints were present in the remaining 15 per cent. In advanced cases

pigmentation was found in 84 per cent, diabetes in 80 per cent and hepatomegaly in 90 per cent. Signs of portal obstruction develop with the progress of the cirrhosis. An enlarged spleen is reported in 60 per cent and ascites is frequently present terminally. No hemolytic disorder has ever been found. Anemia, when present, can be explained by blood loss or iron deficiency.

Signs of sexual hypoplasia, which have recently received a great deal of attention in connection with portal cirrhosis, have always been prominently associated with hemochromatosis. In both of our cases there was sparse hair over the chest and in the axillae and the pubic hair showed a female distribution. Case 1 had diminished sexual desires. Case 2 had complete loss of libido. Of interest are the results of the hormonal assays in these patients. In the male, the 17 ketosteroids are derived from the testes and the adrenal cortex, roughly one-third from the former and two-thirds from the latter[11]. If the 17 ketosteroids are fractionated by digitonin separation into alpha and beta fractions, one finds normally 85-95 per cent alpha and 5-15 per cent beta. This beta fraction, consisting chiefly of dehydroiso-androsterone, is elevated in cases of hyperfunction of the adrenal cortex. It is thought that this component of the urinary 17 ketosteroids is derived from the adrenal cortex. In Case 2 the total ketosteroids were low. Although adrenocortical hypofunction has been suspected as an explanation for many of the symptoms of hemochromatosis, there has been little evidence to support it. Simpson[12] cites 2 cases from the early literature in which the two conditions were coincidental. Cantarow[13] reported a case exhibiting signs of both conditions with corroborative laboratory data. In view of the hypotension, equivocal Robinson-Power-Kepler test, lack of chest and axillary hair, lack of libido and the presence of pigment in the skin in this case, and the common autopsy findings in reported cases of iron-containing pigment in the adrenal cortex, a fractionation of the total neutral 17 ketosteroids was done to determine the relative proportions of the testicular and adrenocortical components. It was found that the beta fraction was definitely elevated (27.1 per cent). This indicated that the contributions from the testes and the adrenal cortex were reduced, with the main reduction occurring in the latter. The presence of an hypogonadism was substantiated by the results of the assay of the urinary gonadotropin (FSH). On two occasions a doubtful reaction was obtained at the level of 80 mouse units per liter. In our laboratory clear cut negatives are found with normal testicular function and doubtful or positives characterize hypogonadism. It may be noted that this finding also excludes an hypophyseal origin of the hypogonadism, which is a theoretical possibility because of the pigment deposit common'y found in the pituitary gland. We are of the opinion that in this case there was hypofunction of both the adrenal cortex and the testes, the latter being more seriously affected. The problem then arises of how to explain the testicular deficiency. A generally held theory is that the liver inactivates estrogens[14,15] and the diseased liver loses this ability[16,17,18], which in turn causes inhibition of testicular activity. However, in the subject of this report the estrogens were not

elevated, so that the mechanism is at present unexplained. The common autopsy finding of only mild pigmentary deposit in the testes would fail to support the theory of testicular fibrosis causing the hypogonadism. No hormonal abnormalities were found in Case 1. This is in keeping with the clinical picture which was much less advanced than Case 2.

Diagnosis:—The diagnosis can be made clinically in advanced cases in the presence of diabetes, bronze pigmentation of the skin, hepatosplenomegaly and evidence of hypogonadism. However after analysis of the figures given by Sheldon[1], Humphrey[2] and many individual case reports, and in our Case 1, it is seen that hemochromatosis may exist without these classical features. In such cases the finding of pigment cirrhosis by liver biopsy, the presence of hemosiderin, hemofuscin or melanin by skin biopsy, and the finding of hemosiderin in the urine and other body fluids are of the utmost diagnostic importance. It must be mentioned that mild hemosiderosis per se is not of itself diagnostic of hemochromatosis. Hemosiderin is not uncommonly found deposited in organs as a result of blood destruction, e.g., in hemolytic anemia, congestive heart failure, etc.

Prognosis:—In Sheldon's[1] series the average duration of life, from the time the diagnosis of hemochromatosis was established, was 18 months. There are no recent reports of a large series of cases to estimate the present life expectancy but it is quite clear that the figure is considerably higher than Sheldon's. Of the chief causes of death, diabetes, pneumonia and tuberculosis are surely lesser threats today. While diabetes was the cause of death in 50 per cent of Sheldon's series, modern therapy for diabetes has appreciably reduced this figure. Despite his severe diabetes, our Case 2 was adequately controlled with an insulin mixture and diet. With the newer methods in the medical and surgical treatment of portal cirrhosis, and the antibiotic and chemotherapeutic treatment of pneumonia and tuberculosis, we have every reason to expect a longer life expectancy in hemochromatosis. However carcinoma of the liver, which until now has been found as a terminal event in 8 per cent of patients with hemochromatosis, will undoubtedly take a greater toll as the other causes of death assume less importance.

Summary

1. The literature pertaining to hemochromatosis has been reviewed.

2. The newer concepts of pathogenesis have been stressed.

3. The importance of the newer diagnostic methods such as liver biopsy, skin biopsy and hormonal assays in establishing a definite diagnosis have been pointed out.

4. Two cases have been reported. One patient showed no evidence of pigmentation. Neither patient had the progressive uncontrollable diabetes heretofore considered characteristic of hemochromatosis.

REFERENCES

1. Sheldon, J. H.: Hemochromatosis, London, Oxford University Press, 1935.
2. Humphrey, A. A., Alpiner, and Verity, L. E.: Hemochromatosis, Arch. Dermat. and Syph. **45**:1128-1132.
3. McPhedran, W. F.: Hemochromatosis, Tice Practice of Medicine 1940, New York, W. F. Prior Co., vol. 9, p. 57.
4. Butt, H. R., and Wilder, R. H.: Hemochromatosis. Arch. Path. **26**:262, 1938.
5. John, H. J.: Hemochromatosis, J.A.M.A. **112**:2272, 1939.
6. Joslin, E. P.: The treatment of diabetes mellitus, ed. 8, Philadelphia, 1946, Lea and Febiger, p. 547.
7. Strachan, A. S.: Haemosiderosis and haemochromatosis in South African natives, M.D. Thesis, Glasgow, 1929.
8. Gillman, J., and Gillman, T.: Structure of liver in pellagra. Arch. Path. **40**:239, (Oct.), 1945.
9. Herbut, P. A., and Tamaki, H. T.: Cirrhosis of the liver and diabetes as related to hemochromatosis. Am. J. Clin. Path. **16**:640, (Oct.), 1946.
10. Herbut, P. A., Watson, J. S., and Perkins, E.: Alloxan in experimental hemochromatosis. Am. J. Clin. Path. **16**:506, (Aug.), 1946.
11. Fraser, R. W., Forbes, A. P., Albright, F., Sulkowitch, H. and Reifenstein, E. C. Jr.: Colorimetric assay of 17 Ketosteroids in Urine. J. Clin. Endocrinol. **1**:234-256, 1941.
12. Simpson, S. L.: Addison's disease and diabetes mellitus in three patients. J. Clin. Endocrinol. **9**:403-425, 1949.
13. Cantarow, A., and Bucher, C. J.: Hemochromatosis, report of a case. Arch. Int. Med. **67**:333-334, 1941.
14. Segaloff, A.: Intrasplenic injections of estrogens and their esters. Endocrinology. **33**:209, 1943.
15. Engel, P.: Inactivation of ovarian hormones by the liver. Endocrinology. **35**:70, 1944.
16. Glass, S. J., Edmondson, H. A. and Soll, S. N.: Sex hormone changes associated with liver disease. Endocrinology. **27**:749, 1940.
17. Talbot, N. B.: Inactivation of endogenous estrogens by the liver. Endocrinology. **25**:601, 1939.
18. Biskind, M. S. and Shelesnyak, M. D.: Effect of Vitamin B-complex Deficiency on Inactivation of Ovarian Estrogens in the liver. Endocrinology. **30**:819, 1942.

RESULTS OF PEPTIC ULCER TREATMENT WITH PROTEIN SUPPLEMENTS *

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Since the introduction of protein hydrolysate supplementary feedings in the treatment of peptic ulcer by Levy and Siler[1] and Co Tui, et al[2], this new form of dietary therapy has received numerous reports of therapeutic effectiveness by Vinci, et al[3], Hodges[4], Kimble[5], Kenamore, Lonergan and Shy[6], Lopusniak and Berk[7], Samis and Hollander[8], Rossien [9], and others. Criticism has also been levelled against the use of this dietary supplement by Sappington and Bockus[10], and others on the grounds that protein hydrolysates offer no advantage over whole protein such as skim milk powder in the treatment of peptic ulcer, because of unpalatability and expense. The whole protein supplement herein described is the first product among those available in pharmacies, to the author's knowledge and experience, which was marked by complete continued patient acceptance and unusual palatability. The superior buffering action of protein supplements has been demonstrated by Levy[12], Lopusniak and Berk[7], Samis and Hollander[8] and others.

All the reports quoted above by the clinical investigators who have tested the clinical and biochemical action of protein hydrolysate in peptic ulcer have employed patients who were hospitalized in almost all cases. These, therefore, represented severe cases of peptic ulcer, who were so acutely ill as to require hospitalization. Since the great majority of peptic ulcer patients are seen first as ambulatory cases, in the doctor's office, it was felt of interest to test the clinical and biochemical reaction to synthetic milk protein feedings given to ambulatory ulcer patients seen in gastroenterologic office practice. None of these patients described herein were confined to bed. Some rested at home, while others ingested their feedings while at work.

The protein supplement used in this study† consisted of 60 per cent protein, 1.5 per cent fat, 27 per cent carbohydrate, 6.3 per cent minerals, and 5 per cent moisture; the protein content is derived principally from the milk proteins casein and lactalbumin, and a small portion from egg albumin and soy bean. The carbohydrate consists mainly of lactose; the iron content is 1.5 mg. per 100 grams; and the sodium content is 0.8 per cent.

Twenty patients, who consulted the author in his office, are presented. Each patient had a chronic peptic ulcer history which ranged from 4 months to 18 years; each case had a proven gastric or duodenal ulcer as shown by x-ray studies. In every instance the x-ray films showed an ulcer crater, or constant duodenal cap deformity, or persistent ulcer fleche or niche with associated duodenal cap deformity, cap spas-

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†The protein supplement used in this investigation was H.P.S. Sixty (High Protein Supplement 60%) supplied by The Wander Company of Chicago.

TABLE I

DESCRIPTION OF CLINICAL MATERIAL AND RESULTS OF PEPTIC ULCER THERAPY USING PROTEIN SUPPLEMENT OF CASEIN.

Case No.	Age & Sex	Type of Ulcer	Duration of Symptoms (Years)	Complications	Duration of Therapy (Days)	Symptom Relief Days Required	X-ray Findings Before Therapy	X-ray Findings After Therapy	Weight Gain (lbs.)	Comments
1.	44 M	Duo.	2	0	21	2	Crater, cap spasm and irritability	Crater disappearance. No spasm.	8	No recurrence after placing on bland diet (mod. Sippy).
2.	37 M	Duo.	1	0	14	1	Ulcer niche cap spasm & irritability	Niche & assoc. signs disappearance	10	No recurrence when placed on mod. Sippy regime.
3.	56 M	Duo.	8	2 Bouts of Hematemesis	21	3	Cap deformity (cauliflower), spasm & local pain.	Deformity unaltered; spasm & pain gone.	0	Placed on bland diet with mid-meal hydrolysate feedings—3 months.
4.	40 F	Gast.	0.3	0	14	1	Crater 4 mm. x 6 mm. lesser curvature.	Disappearance of ulcer crater.	3	(vd. Supra #3)
5.	61 M	Duo.	9	Recurrence of Vomiting	21	5	Penetrating ulcer; gastric delay in emptying.	No evidence of active ulcer; normal emptying.	2	(vd. Supra #3)
6.	29 M	Duo.	1	0	14	1	Cap crater with spasm, pain & irritability	No evidence of ulcer seen.	8	(vd. Supra #2)
7.	48 M	Pyloric	18	Recurrent Vomiting	14	0 No relief	Penetrating Pyloric Ulcer Crater.	No change	−7 (loss)	Subtotal gastrectomy performed.

(Table I Continued)

Case No.	Age & Sex	Type of Ulcer	Duration of Symptoms (Years)	Compli-cations	Duration of Therapy (Days)	Symptom Relief Days Required	X-ray Findings Before Therapy	X-ray Findings After Therapy	Weight Gain (lbs.)	Comments
8.	33 M	Duo.	3	0	21	3	Cap deformity, tenderness & spasm.	Deformity same, tender-ness & spasm gone.	1	(vd. Supra #3)
9.	47 F	Gast.	0.5	Recurrent Vomiting	14	4	Crater 1 x 1 cm. antrum lesser curva-ture; Marked pylorospasm.	No evidence of crater. No pyloro-spasm noted.	3	(vd. Supra #3)
10.	30 M	Duo.	2	0	14	2	Cap fleche, local pain spasm & irritability	No evidence of fleche; pain & spasm & irrita-ability gone.	4	(vd. Supra #3)
11.	55 M	Duo.	8	Recurrent Melena & Hematemesis; Vomiting	21	0 (No relief)	Cap deformity (clover-leaf), pyloric ob-struction.	Unchanged	-5 (loss)	Subtotal gastrectom performed.
12.	22 M	Duo.	0.3	0	7	1	Ulcer niche, local tender-ness & spasm.	No evidence of niche; tenderness & spasm gone.	5	(vd. Supra #3)
13.	41 M	Duo.	4	Recurrent Retention Vomiting	21	3	Cap deformity (cauliflower) pylorospasm & gastric reten-tion.	Deformity same; no gastric retention; no pylorospasm.	10	(vd. Supra #3)

(Table I Continued)

Case No.	Age & Sex	Type of Ulcer	Duration of Symptoms (Years)	Complications	Duration of Therapy (Days)	Symptom Relief Days Required	X-ray Findings Before Therapy	X-ray Findings After Therapy	Weight Gain (lbs.)	Comments
14.	49 F	Duo.	10	0	21	2	Crater, spasm & irritability.	Disappearance of crater, spasm & irritability.	4	(vd. Supra #3)
15.	44 M	Duo.	3	0	10	1	Cap niche spastic deformity & local pain.	Normal Cap.	2	(vd. Supra #3)
16.	60 M	Gast.	0.5	0	18	1	Crater 1x1 cm. lesser curvature angularis.	Disappearance of ulcer crater.	6	(vd. Supra #2)
17.	40 M	Duo.	1.5	Melena on one occasion	14	1	Cap crater small size, with deformity (spastic).	Normal Cap.	0	(vd. Supra #3)
18.	52 M	Duo.	15	0	21	6	Cap deformity and delay in gastric evacuation.	Deformity same; normal gastric evacuation.	8	(vd. Supra #3)
19.	26 M	Duo.	0.3	0	7	1	Cap fleche, with pain spasm & irritability.	Normal Cap.	5	(vd. Supra #3)
20.	38 M	Duo.	25	0	14	2	Crater, spasm, tenderness & irritability.	Normal Cap.	0	(vd. Supra #3)

ticity, irritability, and cap tenderness to local palpation under fluoroscopic guidance. Every individual had active ulcer symptoms at the time of the office visit, having had ulcer symptoms intermittently as described in Table I. No patient had extragastric or extraduodenal disease, and no patient was seen during an acute hemorrhage, or in acute pyloric obstruction.

Of the 20 patients, 17 were males, 3 were females; the ages varied from 22 to 61 years of age, as noted in Table I. There were 3 gastric ulcers, 1 pyloric ulcer, and 16 duodenal ulcers. Three patients had a history of previous hematemesis and/or melena, none of whom were bleeding at the onset of protein supplement therapy. Four patients gave a history of previous retention vomiting, and each of these individuals had retention vomiting when first seen and at the onset of protein supplement treatment.

Gastroscopic visualization of the gastric ulcer was done in cases 4, 9, and 16. Gastroscopy suggested the benign character in each of these cases; gastroscopy was

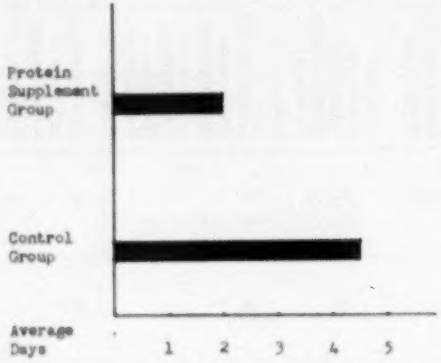

Fig. 1—Comparison of therapy with protein supplement and sippy dietary regime in time needed for relief of ulcer pain.

confirmatory of ulcer crater disappearance along with the x-ray report in each case as well.

On the day following the x-ray studies and the gastric analysis, the patient was placed on the following protein supplement feedings exclusively, with the exception of a mineralized vitamin tablet which supplied all necessary vitamins and minerals. A one and one-half ounce feeding of the supplement was taken every one and one-half hours in 6 ounces of milk or water.

If the patients required night feedings these were ingested as needed. No other food was taken during the day other than the protein supplement feedings. The feedings were given from 7 to 21 days, most patients taking from 2 to 3 weeks of the exclusive supplement feeding therapy; at the expiration of this time, the patient was placed (Table I) on a diet for periods up to 3 months in most cases which was bland and aided by an in-between meal feeding of the supplement in milk or water

as desired by the patient. In an occasional instance the patient preferred to have only a mid-meal feeding of milk alone, or to do without this feeding and to take an antacid alumina hydroxide gel or sedative-antispasmodic preparation for greater digestive comfort.

A gastrointestinal x-ray series was taken in each case immediately before the onset of, and immediately after the cessation of the exclusive protein supplement feedings. In addition, each patient had various blood studies made before and after treatment, consisting of the blood urea nitrogen, serum albumin and globulin, hemoglobin and hematocrit readings.

Before treatment, a gastric analysis was performed using a modified histamine technic to measure the buffering action of the supplement in the method similar to that described by Levy[18]. The histamine was injected subcutaneously as 0.1 mg. per

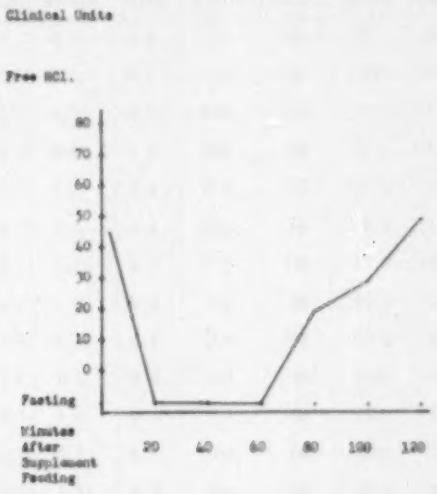

Fig. 2—Graphic demonstration of typical gastric acid response to protein supplement feedings.

10 kilo body weight on a fasting stomach in the morning after the fasting gastric contents were evacuated immediately following which 300 c.c. of a 10 per cent solution of the supplement were ingested. Aspirations were taken thereafter every 20 minutes for 120 minutes. The gastric contents were tested for free acid by titrations with N/10 Sodium Hydroxide, employing Toepfer's reagent as indicator.

Findings

The relief of ulcer pains was effectively achieved on an average of 48 hours in these patients, and was striking in its superior therapeutic action to the patients who had been on previous ulcer regimes. As shown in Fig. 1, the time required for pain relief was approximately one-half that required for relief of pain on the regular modified Sippy ulcer regime. In Fig. 1, these latter 20 control patients were taken

from practice and a previous report by Morrison[12]; these control cases were also seen as office patients, and were similar in all respects to the patients treated with supplement.

The changes in blood urea nitrogen, fractional proteins, hematocrit, and hemoglobin readings as described in Table II, before and after treatment with the protein supplement, were not statistically significant in this series of patients.

TABLE II

SERUM PROTEIN, BLOOD UREA, HEMOGLOBIN RESPONSE BEFORE AND AFTER TREATMENT WITH PROTEIN DIETARY SUPPLEMENT.

Case No.	Hematocrit		Hemoglobin Grams %		Serum Albumin Grams %		Serum Globulin Grams %		Blood Urea Nitrogen mg. %	
	Before	After	Before	After	Before	After	Before	After	Before	After
1.	43.5	44.8	82	80	4.5	4.9	3.0	3.3	14	15
2.	47.5	46.0	102	96	4.7	4.5	2.8	2.6	13	19
3.	47.1	44.5	58	66	4.3	5.4	2.6	2.9	24	15
4.	39.1	41.5	83	85	4.8	4.9	3.0	2.5	11	12
5.	40.0	51.2	72	75	4.0	4.9	2.7	3.1	19	14
6.	48.8	46.5	83	81	4.2	4.6	2.5	2.9	18	29
7.	39.2	42.8	77	80	5.2	4.8	2.3	2.6	19	22
8.	47.5	45.2	96	95	4.3	4.9	3.1	2.8	15	18
9.	32.5	38.8	69	80	4.4	4.2	2.6	2.5	11	15
10.	45.6	44.0	106	101	4.6	4.4	2.8	2.9	10	12
11.	38.4	47.2	55	63	4.2	4.9	2.4	2.4	26	13
12.	50.0	47.7	105	100	4.8	5.2	3.0	2.9	13	11
13.	33.3	42.0	80	82	4.0	4.8	2.8	3.4	18	20
14.	40.8	40.2	73	77	5.0	4.7	3.5	3.2	17	26
15.	51.5	50.6	96	95	5.5	4.9	3.1	3.4	14	18
16.	40.2	46.3	82	83	4.7	4.5	2.7	2.3	21	20
17.	52.4	47.0	62	68	4.4	4.2	2.5	2.4	22	16
18.	51.0	51.4	85	82	4.5	4.8	2.6	2.7	23	20
19.	50.0	49.6	105	103	4.0	4.4	3.1	3.2	12	13
20.	44.6	46.8	98	100	4.7	4.6	2.5	2.5	11	17

The x-ray findings in each case, described in Table I were such as to indicate complete disappearance of the ulcer crater, fleche, niche, spasm, irritability, etc., at the expiration of the treatment period in 2 or 3 weeks. Two exceptions occurred,

cases 11 and 7, who had been intractable to previous Sippy regimes and who likewise failed to respond to the hydrolysate treatment. In these 2 cases, surgery was performed in each, a subtotal gastrectomy being required.

The results of the buffering tests on gastric acidity during the histamine gastric analyses revealed that the protein supplement completely buffered the free acidity

TABLE III

NEUTRALIZING EFFECT OF PROTEIN SUPPLEMENTS ON GASTRIC ACIDITY IN PEPTIC ULCERS.

(Units of Free HCl)

Case No.	Fasting Specimen	Interval following protein supplement feeding (minutes)					
		20	40	60	80	100	120
1.	45	0	0	0	18	26	46
2.	60	0	0	8	35	62	75
4.	22	0	0	0	0	10	28
5.	33	0	0	0	0	16	36
6.	55	0	0	0	30	42	58
7.	24	0	0	0	0	0	35
8.	30	0	0	0	0	18	42
9.	16	0	0	0	0	0	12
10.	43	0	0	0	20	38	32
12.	36	0	0	0	0	10	16
14.	32	0	0	0	0	21	44
15.	18	0	0	0	0	0	26
16.	39	0	0	0	0	14	32
18.	27	0	0	0	0	0	38
19.	43	0	0	0	24	36	48
20.	76	0	0	16	46	68	112

in every case listed in Table III, except for cases 2 and 20, which showed free acidities of 8 and 16 clinical units respectively at 60 minutes. The majority of cases also were shown to have a complete buffering action at 80 minutes as well. At 100 minutes, however, the majority of patients revealed a substantial rise in gastric acidity which increased at the 120 minute extraction. Fig. 2 is a graphic demonstration of a typical gastric acid response to the protein supplement feeding following histamine

injection. It may be that the buffering action of the supplement would be prolonged if milk instead of water were to be used as its vehicle.

The speed of ulcer healing in this series is in sharp contrast to the longer time required in the conventional ulcer treatment. This series took approximately half the time usually required for ulcer healing on the conventional ulcer regimen, as described by Cummins, Grossman, and Ivy[11] who found an average of 41 days required for roentgen evidence of ulcer crater healing in duodenal and gastric ulcers treated by current modifications of the Sippy regime.

Sappington and Bockus[10] have recently drawn attention to the negative nitrogen balance which is so prone to exist in the chronic peptic ulcer case. Protein supplement therapy would appear to restore a positive nitrogen balance effectively in chronic peptic ulcer. The importance of adequate protein reserve in wound and ulcer healing is well known and has been emphasized by Elman[12], Co Tui[14], Ravdin[15], and Stare and Thorn[16]. Protein supplement appears to be especially suited to supply this protein need in ulcer patients. Most patients gained weight, on the protein supplement regimen; those who had been on previous conventional ulcer treatment remarked particularly about their unusual sense of well being while taking the supplement.

Summary

1. In a series of 20 patients with chronic peptic ulcer who were ambulatory and seen in gastroenterologic office practice, the oral feedings of a protein supplement mixture for periods up to 3 weeks resulted in the following:

A. The time required for relief of pain was half that noted on the conventional modified ulcer Sippy regime.

B. The time required for x-ray evidence of ulcer healing was approximately half that seen on the conventional modified ulcer Sippy regime.

C. The buffering, antacid action of the mixture is such that a therapeutic feeding is effective in most cases of maintaining a gastric achlorhydria for an average of 80 minutes.

2. The palatability and patient acceptance of the protein supplement was striking, the mixture being accepted without reservation by patients.

3. A protein supplement was found to be a highly effective superior therapy in the dietary treatment of chronic peptic ulcer.

References

1a. Levy, J. S. & Siler, K. A. Am. J. Digest. Dis. **9**:354, 1942.
1b. Levy, J. S. Gastroenterology. **6**:883, 1948.
2. Co Tui, F., Wright, A. M., Mulholland, J. H., Gavin, T., Barcham, I., and Gerst, G. R. Gastroenterology. **5**:5, 1945.
3. Vinci, V. J., Speight, H. E., La Bella, L. O. and Buckley, W. E. Conn. State M. J. **10**:281, 1946.
4. Hodges, H. H. Gastroenterology. **8**:476, 1947.
5. Kimble, S. J. Gastroenterology. **8**:467, 1947.
6. Kenamore, B., Lonergan, W. and Shy, J. C. Gastroenterology. **10**:177, 1948.
7. Lopusniak, M. S. and Berk, J. E. Gastroenterology. **6**:891, 1948.
8. Samia, S. M. and Hollander, F. Gastroenterology. **12**:665, 1949.

9. Rossien, A. X. Am. J. Digest. Dis. **14**:205, 1947.
10. Sappington, T. S. and Bockus, H. L. Ann. Int. Med. **31**:271, 1949.
11. Cummins, G. M., Grossman, M. I. and Ivy, A. C. Gastroenterology. **7**:20, 1946.
12. Morrison, L. M. Am. J. Digest. Dis. **12**:325, 1945.
13. Elman, R. and Lescher, C. Surg. Gynec. & Obst. **76**:503, 1943.
14. Co Tui, F. Bull. N. Y. Acad. Med. **21**:629, 1945.
15. Ravdin, I. S. Ann. Surg. **112**:576, 1940.
16. Stare, F. J. and Thorn, G. W. J.A.M.A. **127**:1120, 1945.

PSYCHOSOMATIC PROCTOLOGY

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Introduction

Psychosomatic proctology is proctology. This brief statement provides a simple and yet profound definition. Any consideration of the surgical aspects of proctology is merely that and nothing more. It is partial, incomplete, one-sided. A study of the medical aspects of proctology is equally incomplete. A presentation of the "emotional" aspects of proctology results in still another unfinished picture. In its basic meaning psychosomatic proctology includes all of these. It is a more complete presentation.

The physician who treats "disease" without the realization that "disease" is merely the reaction of a human "body" and "mind" to the presence of a disturbing factor or factors in the internal or external environment of that "body" and "mind" is slowly becoming outdated. The modern physician realizes that the terms "body" and "mind" are artificial separations from the facts of life. The fact is that the mind cannot exist without the body. The fact is that the body and mind are one in their reactions. To attempt to divorce "mind" and "body" in the living organism results in a linguistic deception. Separate labels such as these may be employed for convenience of discussion, but they may not be employed unless we realize that they are labels and nothing more. They cannot be employed unless we understand that they do not represent the facts. The fact is that the body and mind are inseparable in the life functions. They are thus inseparable in the reaction of the body-mind to internal environmental or external environmental irritants such as bacteria, pollen, etc. This reaction is known as "disease".

In psychosomatic proctology we deal with reactions of the body-mind which manifest themselves chiefly in and about the colon, the rectum and the anus. However, the physician will readily understand that everything we will have to say with regard to psychosomatic proctology may be applied with equal profit to a consideration of all other fields of medicine. Just as the mind and the body cannot be disassociated, so proctology cannot be separated from any other field of medicine. The proctologist must see his patient in the entirety. So must the internist, the urologist, the dermatologist, the general surgeon, the cardiologist, etc., etc. Thus, the material herein contained may be read with profit by all physicians, and applied immediately regardless of their field of medical endeavor.

The patient with a cancer phobia relating to the rectum reacts no differently than the patient with a cancer phobia relating to the lungs. The patient who presents evidence of anxiety neurosis involving pruritus or colon hyperactivity as one of the somatic manifestations is essentially the same patient as the one who presents a cardiologist with palpitation and dyspnea on a psychosomatic basis. Each requires the same understanding, the same explanation, the same opportunity for integration.

The patient with "semantic twist" who reacts to the word "colitis" as if it meant "cancer" is no different from the patient who reacts to the words "coronary disease" as if they meant "sudden death". Both patients require a re-education in the evaluation and meanings of words. The patient who feels that the diagnosis of "tumor" means "cancer" will apply this meaning in his body reactions whether we are dealing with a tumor of the colon or a tumor of the brain. The psychotherapeutic measure provided by a study of general semantics will dispel the anxiety in these cases. The technic of general semantics is equally well applied by physicians in all branches of medicine.

The preface to the author's textbook, "Ambulatory Proctology" includes the following sentences:

"The truly capable proctologist must be well versed in both conservative and radical technics. He must know the medical management of his field, and both the conservative and radical operative approaches. Whether or not he employs ambulatory technics exclusively, he should be master of these methods so that he may freely choose his approach in each case. Unfortunately many physicians are lop-sided in their development. They are either medically trained or surgically trained. Thus, the patient's treatment is predetermined by the physician's training and inclination, and not by the needs and peculiarities of the individual case."

We may now add to these sentences. Unless the proctologist is trained to think in psychosomatic terms he will be equally lop-sided both in his diagnosis and in his therapy. His surgical technic in performing a hemorrhoidectomy may be faultless. His operation of tattoo-neurotomy may be cleverly performed in the treatment of pernicious pruritus ani. However, if he overlooks the anxiety neurosis upon which the symptoms and physical findings are ultimately based, his patient will continue to "suffer" and will seek elsewhere for relief. The technics of psychosomatic proctology are not difficult. They are mastered simply for they all follow naturally, *once the physician has accepted a point of view.*

I must here introduce a word of caution. Just as it is exceedingly important for the physician to realize the part played by the psyche in the production of "disease", so it is equally important that the role not be overstressed. It is an important role, and sometimes a leading role, but it must not be allowed to over-shadow the parts of the other players in the drama of "disease".

Psychopathology

Psychosomatic proctology, therefore, concerns itself with the study of patients who present symptoms referable to the colon and rectum without discoverable organic disease. The importance of this field is indicated by the statistical fact that 25 to 45 per cent of all colon complaints are without organic background. These patients represent so-called "functional problems".

It must be further recognized that another very large group of proctologic patients presents symptoms that are partly the result of emotional factors. In other words, even though an organic background is found, an emotional factor complicates

or exaggerates the organic disease process and symptoms. Still another group of proctologic patients presents a picture that begins on an emotional basis and subsequently becomes complicated by organic factors. It is important to recognize these latter groups of cases.

Still further, many of the diseases of the autonomic nervous system are proper studies of psychosomatic proctology. More and more we recognize the relationship of the psyche to allergic manifestations. Allergic colon disorders are not uncommon.

We must understand that the emotional factors can produce actual structural changes. The sequence of events is a psychological or emotional disturbance resulting in a functional change, which in turn produces a structural or cellular disease. This does not mean that every case classified under the term "psychosomatic proctology" is entirely of psychogenic origin. Many of the cases will demonstrate an original organic background. Many will demonstrate merely an initiating emotional background, the major clinical evidences being the result of organic superimposed, but otherwise unrelated, factors. For example, an emotional factor may initiate a diarrhea. As a result of the constant irritation of the mucosa produced by the hypermotility of the colon, bacteria may assume the secondary role of invaders. Subsequent disease processes may be chiefly the result of the bacterial invasion. In this case, the emotional factor did not produce the ulcerations we saw clinically, but was merely an initiating cause. The patient cannot be properly treated until the psychological factors, furnishing the background of the functional impairment, are determined. We must not treat the disease. We must treat the patient.

In this presentation I will not enter into a detailed discussion of the diseases with psychosomatic background. I am merely concerned with the introduction of the concept. We will thus be content with a listing of the pathology associated with or resulting from emotional disturbances.

Such pathology includes: 1. Mucous colitis, 2. Ulcerative colitis, 3. Pathology subsequent to psychogenic constipation or diarrhea, 4. Pruritus ani, 5. Colon motor neuroses, 6. Coccygodynia—nontraumatic, 7. Proctalgia fugax, 8. Certain cases of foreign bodies and rectal trauma.

Once more I must emphasize the fact that all cases of mucous colitis or ulcerative colitis or pruritis ani, etc. are not psychogenic in origin. Many are psychogenic, many are partially related to the emotions, and many develop emotional content after initial organic etiology. In any event the great majority of these cases belong to the realm of psychosomatic proctology.

Diagnosis

How are we to recognize a functional disturbance? Are we to make the diagnosis simply by excluding all organic disease? We must remember that in most diagnostic problems there will be both a functional and an organic component. It is merely a matter of determining which is the predominant factor, and how each fits into the picture. When this is done, the patient can be properly treated.

To recognize the functional illness we must study the patient's personality and his emotional life. We must know the patient's early as well as his present emotional history. We must understand his reactions, his conflicts. This may not seem a proper study for a proctologist, but it is.

I must add, however, that if the proctologist does not wish to undertake this study he should not therefore neglect it. The psychiatrist is a willing consultant. To ignore the emotional background does not heal the disease.

I should like to present a chart that I have devised for the study of patients' emotional life in its bare fundamentals. This chart is called a *"Conflict Check Chart"*.

Emotional Conflict Check Chart

By means of this list we will review the major causes of conflict. Be very honest in checking. In the checking pretend that you are the diagnostician, and look at yourself as if you were another person,—the patient.

Infancy and Childhood

1. Record your earliest childhood memory.
2. Excessive coddling.
3. Excessive affection, with every whim gratified.
4. Discouraged initiative.
5. Strict regimentation.
6. Strict religious training.
7. A strong sense of sin and guilt.
8. Demanding, possessive parents.
9. Parents discussed illness and other problems in your presence.
10. Constant wrangling and arguments between parents.
11. Constant conflict as to which parent is to be obeyed.
12. Setting of other children on a pedestal, as examples for you.
13. Over-discipline, with no choice of conduct offered to you.
14. Discipline by fear and punishment.
    a. Physical.
    b. Emotional—sin.
15. Teaching that sex is sinful.
16. Lack of information, poor information, or misinformation on sex questions when raised by you.
17. Parents stayed together for your sake.
18. Were you an only child?
    a. Coddled.
    b. No competition.
    c. No self-reliance.
    d. Never learned to share with others.
    e. Remained attached to mother or father to an unusual degree.
19. Envy of second child
    a. Were you made to feel less important when the other child arrived?
    b. Was the competition too difficult?
20. Were you an unwanted child?

Adolescence

1. Over-critical parents.
2. Parents posed as paragons of virtue.
3. Did you think of your parents as paragons of virtue and were you disillusioned?
4. No free choice of opinion and course of action.
5. Over-discipline.
6. Pretended or actual illness of parent to hold you close to home.
7. Unpleasant home atmosphere.
    a. Constant bickering.
    b. Pessimistic parents.
    c. Lack of economic security.
    d. Marital incompatability of parents.
    e. Unsatisfactory neighborhood or other environment.

8. Ridiculed during awkward stage of adolescence.
    a. Were you made to feel self-conscious or inferior?
9. Rigid religious instruction.
10. No sex instruction.
11. Street corner sex instruction.
12. Sex instruction by obscene literature.
13. Unsatisfactory sex experience with your own sex.
14. Unsatisfactory sex experience with the opposite sex.
15. False modesty with regard to sex.
    a. Demonstrated by parents.
    b. Demonstrated by teachers.
    c. Demonstrated by religious leaders.
    d. Demonstrated by companions.
16. Attitude toward masturbation.
    a. Told that it was normal.
    b. Told that it was a sin.
    c. Told that it would lead to mental deterioration.
    d. Told that it would lead to physical deterioration.

Adult Life

1. Marital problems.
    a. Was your marriage an escape from an unsatisfactory home environment?
    b. Did you marry for money?
    c. Did you marry because of puppy love?
    d. Was your love entirely physical?
    e. Nothing in common with your mate.
        1. Intellectually.
        2. Emotionally.
        3. Spiritually.
    f. Did your family force this marriage?
2. Are you bored with your mate?
3. Do you constantly seek escape from home?
    a. Lodges.
    b. Other social activities.
    c. Out with the boys.
    d. Bars and Grills.
    e. Night clubs, and so forth.
4. Sex needs unsatisfied.
5. Inability to satisfy sex needs of your partner (or vice versa).
6. Your temperaments differ.
    a. You are optimistic and your partner is a pessimist.
    b. You like the company of others and he prefers to be alone.
    c. You need affection and he is indifferent.
7. Your mental level is higher or lower than his.
8. Your religious beliefs are different from his.
9. You have a child and there is a question as to what the religious training should be.
10. Your ideas on training your child in all respects differ from those of your partner.
11. You have no children and don't want any although your partner does (or the reverse).
12. You don't feel a need for your mate.
13. Your mate feels no need for you.
14. You have no common interests either in his business or elsewhere.
15. You do not enjoy sharing your experiences and activities.
16. Your in-laws are troublesome.
17. There are financial difficulties.
18. Sudden wealth led to a change in attitude.
19. You know nothing of the anatomy of sex.
20. You know nothing of the physiology of sex.
21. Your partner knows nothing of the anatomy or physiology of sex.
22. You do not enjoy the sex act.
23. Your partner does not enjoy the sex act.
24. You indulge in it merely for the satisfaction of your partner.
25. You pretend to enjoy it but you do not have an orgasm.
26. All that you know about sex you learned at bridge parties or from your friends.
27. The sex act gives you a feeling of guilt.
    a. Due to misinformation.
    b. Due to strict religious training.
    c. Sex is a sin.

28. You believe that you are frigid and that your partner is impotent.
29. Your husband ejaculates prematurely before you get any satisfaction.
30. You have consulted a physician in the matter of sex life.
31. Your partner has consulted a physician in the matter of sex life.
32. You fear pregnancy.
33. You fear venereal disease.
34. You fear that your partner is or has been promiscuous.
35. You feel that your partner is dissatisfied with you sexually.
36. You are dissatisfied with your partner sexually.
37. Your partner is not physically clean.
38. You are not physically clean.
39. There is insufficient by-play in the sex act.
40. You are always tired when the sex act is performed.
41. Intercourse is always associated with argument or nagging.
42. You feel that the sexual demands of your partner are perversions.
43. You have a physical defect that bothers you.
    a. Large ears.
    b. Large nose.
    c. Receding chin.
    d. Pendulous breasts, and so forth.
44. You have been rejected in love.
45. The death of mother or father plunged you into despair and depression.
46. You lost money.
47. You lost your job.
48. You did not receive the advance you expected.
49. Your children are not developing as you feel they should.
50. You have more troubles than anyone.
51. List here any recent acute source of worry.
52. Your mate is losing interest in you and this illness is an opportunity to keep him at home.
53. Someone is more attracted to your mate and your illness will hold his attention.
54. Your illness prevents your child from leaving home and that is just what you want.
55. Your illness makes it hard on some member of your family and you'd like to revenge yourself on that person.
56. You find it hard to get a job and your illness offers an easy explanation.
57. You like to have someone else support you.

Now that you have filled in the check list go back over it and see if you have been entirely honest. If you feel that there should be any changes made, make them. Now present the check list to your physician for his study and evaluation. Discuss the factors involved with him. Withhold nothing. Remember that only by an honest and complete discussion can you arrive at a proper solution for your difficulties.

This check chart may be presented to the patient with the following instructions. He should be told to answer the questions as carefully and extensively as possible. Of course he is advised that it is absolutely impossible to completely unearth all emotional factors as a consequence of this study. That will require the careful and extended study of a psychiatrist.

The hope, in the use of the chart, is to make the patient fully aware of the psychogenic factors in the background of his illness. It is merely a jumping-off point for complete study. In some cases, of course, it will suffice and be complete in itself.

However, in those cases with a strong emotional background, deeply rooted, it will be necessary to seek consultation with a psychiatrist. This is to be expected and anticipated. However, it is often better to lead into this gradually rather than to refer the patient immediately.

Therapy

In this presentation I will make no effort to discuss the therapy of the patient with a strong emotional background. In some cases, however, the completion of

the Check Chart will be sufficient to provide an emotional catharsis and relief from symptoms. In many cases, however, more extended psychotherapy is indicated. This will require the services of a consultant psychiatrist.

There are certain modalities of psychotherapy that can be employed by the proctologist. However, that will be the subject for another discussion at a later date. It is my purpose, in this paper, merely to emphasize the tremendous implications of psychosomatic proctology. If the proctologist is made aware of the psychogenic background of many of his problems this paper will have served its purpose well.

Conclusions

The term *psychosomatic proctology* is offered as an all-inclusive term to cover all phases of proctology—surgical, medical and emotional. The physician must realize that disease of the colon is merely the reaction of the human "body" and "mind" (indivisibly) to the presence of a disturbing factor or factors in the internal or external environment of that "body"—"mind".

The importance of semantics is discussed briefly. The effort here is to present a *point of view*.

Psychopathology of the colon and rectum is described. The sequence of events in the development of structural changes from initial emotional disturbances is related.

The pathology resulting from emotional disturbances includes mucous colitis, many cases of ulcerative colitis, psychogenic constipation or diarrhea, pruritus ani, colon motor neuroses, coccygodynia of nontraumatic origin, proctalgia fugax, and certain cases of foreign bodies and rectal trauma. This list is not intended to be complete.

The diagnosis of functional colon disturbances is discussed, and a new chart for the study of the patient's emotional life is presented. This chart is called a *"Conflict Check Chart"*.

CORTICODIENCEPHALIC GASTROINTESTINAL SYNDROMES IN EPILEPTICS*

(Part XI)

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In the abdominal syndrome group we will offer cases of hemiplegia, and present them in such simple fashion, so that the average internist will see that our localization is exact, since the paralysis in some of the cases is of the cerebral kind and not of the midbrain, pontine, or bulbar types. The first case which we offer to present, deals with extensive brain involvement, but this is essentially cerebral as may be seen from the following data:

L. N. is an adult male, 25 years of age at the time of study. The onset of his epilepsy was at 6 years of age, and the duration of the disease was given as 19 years at the time of the examination. The patient's chief complaints are epilepsy, a paralysis of the extremities and an aura which refers to the abdomen, consisting of a funny feeling and of pain.

The patient was born in January 1913 and his delivery was natural. He was breast fed. Teething began at the age of four months, walking at 13 months, and talking at 18 months of age. He entered school at the age of 5 years and progressed up to the fourth grade. Other diseases, excluding epilepsy, which he was said to suffer from prior to his entry into the institution, consisted of scarlet fever, diphtheria, pertussis, poliomyelitis and syphilis.

His attacks take place both at night and during the day and are invariably preceded by a funny feeling, as well as pain in the stomach. His epileptic attacks have been occurring frequently prior to his admission to the institution. The average number of epileptic attacks he suffered daily, was said to be five.

There was very little in the record regarding elaborate neurological findings at the time of admission. This was not necessary to be emphasized, since even the appearance of the patient disclosed that we were dealing with an organic case of epilepsy in whom the trouble was the cerebrum, since the paralysis plus the history seizures pointed to this portion of the nervous system. Furthermore, this patient's blood Wassermann was positive to the four plus level. Because of his mental retardation, we felt that an attempt at a detailed analysis of the exact nature of the aura and possible associated hallucinatory and other experiences would not be advan-

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tageous in a personal interrogation. We therefore proceeded with the following observations made in the course of a careful neurological reevaluation.

The gait of this patient suggests that he suffers from a paralysis of the right side of the body, since he seems to drag the right lower extremity in walking. When he raises the upper extremities, it is evident that the right one is always lower than the left one, so that he is unable to stretch that extremity and hold it above his head, except partly so, and at an angle, whereas his left one is held straight up. There seems to be, in addition, some limitation in muscle strength on the right, although the patient is not very cooperative. Neither is he reliable enough for a detailed sensory evaluation such as we would like to make in order to determine whether his sensory defect is due to a lesion in the internal capsule or higher up in the cerebral cortex, or in both. Examination of the following few positive reflexes show that the involvement is largely in this patient's left cerebral hemisphere, since, not only is there a definite paralysis of the right side of the body, but it is accompanied by a definite speech defect, thus giving one the false impression that he is very much mentally deteriorated. The following findings on reflex examination are therefore relevant. Although there is no definite increase in the right biceps, triceps, radial and patellar reactions, there is however a definitely positive Babinski reflex on the right side. The reader should be particularly attentive to all our future references to reflex findings, particularly if they differ in one side of the body as compared with those of the other side or in one extremity, compared with those of another extremity. Even if there are no pathological reflexes in the presumably affected extremity, the reflex changes, particularly if associated with some slight muscular weakness, might indicate the existence of an appreciably large intracranial lesion. In future cases we will dwell on reflex changes and stress them, only if paralysis or atrophy are associated with them, but will leave it to the ingenuity of those particularly interested in reflexology to make capital of the localizing significance of reflexes, especially if the remaining clinical findings point to a capsular lesion or to a cortical lesion at the capsule level. For the above reason we made sure to indicate capsular structures of one type or another, in at least eighty per cent of our diagrams. This patient presents some other reflex inequalities as are indicative of general meningeal irritation and do not refer to the lesion in his left cerebral hemisphere. The question of localization applies likewise to the optic atrophy which is present on the right side, and to his facial asymmetry and the atrophy of the posterior portion of his tongue as well as to the fibrillary reaction of the right side of the tongue. It may be that this patient has involvements in other portions of the nervous system than the left hemisphere. These, however, cannot be productive of his epileptic spells. Neither can they be productive of the gastrointestinal reactions which precede the epileptic attacks other than that there is a lesion in the left cerebral hemisphere which is probably large enough to produce the hemiparesis and a secondary hydrocephalus. The lesion might be located anteriorly (see Fig. 64).

The case of patient L. N., presented above, might be elaborated further with regard to the exact localization of the lesion, and his case records might be used to

support either the mammillothalamic or spinothalamic school of thought regarding the origin of neurogenic control of gastrointestinal operations. The case does not, however, present other necessary data which would definitely confine his trouble in either one of the above locations and exclude the other. Furthermore, the patient does not cooperate enough for us to elicit additional neurological evidence. His case record is however very instructive from other standpoints.

The following not uncommon seizure record shows that, in spite of medication with one and a half grains of luminal daily, over a period of years, there was no improvement, either in the frequency of the attacks or in an abolition of the gastrointestinal aura which preceded them. Picrotoxin and creatinin have been mentioned in relation to convulsions with myosis, and phenobarbital, as possibly related structurally to adrenalin, because the former has a cyclic structure in the malonyl urea formula, is also a fact worthy of note. To what extent the corticodiencephalic system operates along the above and similar lines is hard to say. It is evident that there is a great deal to be known physiologically about these structures which are responsible for the autonomic disturbances in the course of the convulsion as well as those which operate to produce the gastrointestinal disturbances preceding it. Our feeling has been that the etiologic diagnosis is just as important as the drug therapy. The former may eventually prove even more important, since syphilis, infections, metabolic and endocrinopathic causes will be seen to be operating as producers of the initial lesion in our cases. In our outpatient clinics we have therefore taken full advantage of laboratory and consultative facilities to establish the underlying causative pathology. The advent of penicillin, streptomycin, endocrine and nutritional advances has widened our scope of the problems uniting phenobarbital with the above. With such a frequency of attacks, the gastroenterologist should not wonder that anything in the way of muscular disturbances in the stomach or intestines could not be possible. We furthermore leave it to the internist to determine whether or not other organs, such as the liver and even the pancreas could also be affected by the constant gastrointestinal spasms incidental to the fits. Percussion of his liver area showed liver dullness of four fingers anteriorly and six fingers posteriorly. Atrophied muscular structures, hypogenetic chondral and osteal elements are items within the neurological armamentarium that need no proof for their existence. Such affected structures hamper the individual in his gait and attitude and make the neurologist or orthopedist very much cognizant of their existence. Sometimes however, muscular and other trophic changes are present in situations that are not accessible to ordinary medical or surgical inspection. This occurs in intrathoracic or intraabdominal atrophies. The presence of these in the thorax and in the upper abdomen we have been able to confirm only on the autopsy table. We have investigated the pelvis of the male and female manually and found these muscular and osseous as well as visceral atrophies. To what extent the liver is affected in this way is hard to say with certainty. Our remarks with reference to the hepatic region should not be taken seriously. Attempt at the production of his fits by

pressure in the carotid region was unsuccessful. We did so in order that we might be able to produce a pattern of attack with special eye and head movements since these would aid in the proper localization of lesions as stressed by Penfield and elaborated upon by us in previous pages from the report of Davison and Goodhart. Although we cannot spend more time on this case with regard to other features, we feel, that a detailed description of the frequency of attacks is essential. The outstanding feature about his seizure record is the fact that the petit mal attacks are almost insignificant in frequency when compared to the grand mal episodes. It is most important that we dwell upon the relationship between petit mal and grand mal attacks in this patient. In the presentation of the seizure frequency of this entire group of syndromes we showed that whenever a patient suffers from a grand mal seizure this is usually associated with petit mal attacks. We did not specifically, at that time, state that the frequency of the petit mal attacks in one individual patient approximates that of the grand mal variety. We know from experience with epileptic patients, that, not only does this frequency of petit mal approximate that of grand mal in any one individual, but that it usually exceeds that of the latter. This is very important from the standpoint of the subject under consideration, i.e., the occurrence of neurogenic gastrointestinal pain. In most patients who suffer from a combination of petit and grand mal epilepsy, the occurrence of the petit mal variety is very common. Not only is it common, but if an aura is associated with the grand mal attacks, it is also associated with the petit mal variety. The detailed description of the seizure frequency in this patient is given with the above emphasis, since we wish that, whenever any discrepancy with respect to the above problem arises with the cases which we will subsequently present, the reader refer to the above remarks and to other similar data at the beginning of every syndrome group. This applies not only to the pain syndrome but to others as well. In this patient the records show 2,080 epileptic spells in a period extending from 1926 to 1938 inclusive; in these there were recorded only 119 petit mal attacks. The reason for so few attacks of the petit mal variety is evident. Usually, when a patient falls in a grand mal seizure, the other patients about him notify the nurse in charge and a record is made of it. This is however not usually the case with the petit mal variety. In spite of this discrepancy with the frequency of seizures, their distribution throughout the various years will be of interest. In 1926 this patient suffered from 94 attacks, of which only 2 were of the petit mal variety. In 1927, 182 attacks were recorded; this was followed by a period of many attacks yearly. In 1928, 188 attacks were recorded; in 1928, 388; while in 1930, 186; in 1931, 182 spells, both petit and grand mal, went on record for this patient. For the remaining years of the seizure record, the numbers of combined grand mal as well as petit mal is as follows: For 1933, 112 fits; for 1934, 114 fits; for 1935, 111 fits; and for 1936, 1937 and 1938, 81, 119, 113 per year respectively. The above make a total of 2,080 fits of which only 119 petit mal fits were recorded. With the progress of the years we can see a slight reduction in the seizure frequency. Whether that was due to the

administration of luminal in larger doses could not be ascertained. When sufficient pneumoencephalographic data will be presented later on in other cases, the reader will be convinced that the following opinion on this case is probably the correct one. We feel that this patient suffered from an initial lesion in one hemisphere caused by a luetic process. In later years the ensuing secondary unilateral hydrocephalus brought about not only the epilepsy but also the vegetative system involvements which manifest themselves in an abdominal aura. It is interesting to note that in 1935 Globus reported on vegetative disturbances of cerebral origin. His report appeared in the February issue of the New York State Medical Journal. In that paper Globus concentrates on disturbances in secondary sexual characters of his patients and in cranial nerve involvements. Because of the latter findings he placed the lesions of his autopsy confirmed cases, in the interpeduncular region. Most of the cases to be presented by us, follow along his pattern of neurological data. We present in addition, more extensive neurological findings, in at least twenty per cent of our cases. His data dealt, however, with the endocrine and not with gastrointestinal systems (Refer to Figs. 62, 63 and 65).

Case L. Mac. N. is a 38 year old woman who was admitted to the institution when she was 23 years of age with a history of epilepsy and athetosis. She also complained of periodic attacks of terrific pain in the abdomen associated with a funny feeling in the head. Her aura of abdominal pain seems to be localized around the navel region. This patient is more interesting than the preceding one because the lesion responsible for her epilepsy and for the gastrointestinal syndrome is localized in the frontal lobe, in its premotor region and probably extends downward into the caudate nucleus.

At this point we can elaborate upon the ideas of Watts and Fulton with regard to the relationship to the extrapyramidal system. We have already said enough with regard to the neuroanatomy of this region. Furthermore, it seems unnecessary for us to stress this premotor region as a place definitely proven by a number of authorities to be the cortical neurogenic center for the control of gastrointestinal movement. There are, however, other points with regard to the work of Watts and Fulton which require emphasis. For this the reader might be referred to the various illustrations which we have presented heretofore. The region referred to above is located in area 6 ab, or thereabout. At present we are mainly interested in presenting the neurological findings in this case, in order to show that the involvement in this patient consists of a lesion which is situated in the cerebral hemisphere near area 6 ab and in no other portion of the brain. The reason for this localization is found in the fact that the athetosis of this patient is on one side and that it is not accompanied by contralateral cranial nerve involvement to it which might be taking it out of the above region and placing it in the mesencephalon, pons or medulla.

The past personal history of this patient is noncontributory other than that she is rather depressed and invariably whines about pain in her right upper extremity. Is such pain thalamostriatal? Her spells are of the grand mal as well as

of the petit mal variety. The neurological examination discloses a patient with a right hemiathetoid gait. Aside from the problem of positive findings that might be overlooked in epileptics as stressed by Muskens, Gowers, and others, we are occasionally faced with a similar situation in patients who suffer from aphasia or mental defect in addition to the epilepsy. Such cases, and even otherwise normal, but young epileptics, are mentally too immature to cooperate for a good sensory evaluation, determination of visual field status or diadochokinetic and acoustic tests. We therefore caution the reader not to underestimate the value of neurologically positive findings that might appear trivial. Illustrating the above statements we present now and will offer in future cases, data on gait, attitude and body position. Sometimes a thorough painstaking examination in such patients will be entirely negative. When the patient walks away from the examiner, the latter will first discover that one extremity is held in the hemiplegic position. She walks with a limp and it is probably the shortening of the right lower extremity which is responsible for this condition. The hemiathetosis involves both the right upper as well as the right lower extremity. It is definitely a hemiathetosis, rather than a hemichorea, since the movements are very slow, resembling even those of a dystonic. Her attitude is that of a half handicapped individual. The Romberg is positive on the right. In spite of the continuous movements of the upper extremity, which would lead one to expect increase in size of its various parts, there is a definite wasting of these parts of the body. Her right palm is atrophied and so is her right forearm as well as her right foot and leg, which is also shortened. The right breast is longer and seems to contain more glandular tissue. The left areola and nipple seems slightly smaller than the right one. With the cases of total or crossed hemiatrophies we have noticed a great many more items than those recorded by Archambault and Fromm or the authorities to whom they referred. Some of this data was verified on autopsy, while others were not. In hemiatrophy of the chest even if it occurred as a single atrophic phenomenon it was accompanied by differences in findings between one side of the chest and the other on percussion and auscultation. We would not want other clinical neurologists to take us to task on this finding, in the same way as the above authorities took Wartenberg and Cassirer and Marburg to task. In operating upon some of these cases in the course of subdural air insufflation one of us (Weingrow) would invariably be on the alert about subjecting such patients with a definitely undermined vital capacity, to the dangers of shock. We could add much more data to this subject of atrophy as uncovered on vaginal and rectal explorations. We feel, however, that the average neurologist might consider such procedures out of his realm. We do not care to make elaborate comments about this phenomenon of crossed endocrine atrophy but reference to our detailed neuroanatomic descriptions of the diencephalon particularly the mammillary will be self-explanatory. We have stressed an abundance of commissural and decussational fibres in this region. Investigators with an anatomical trend, should be able to construct a neurocrine syndrome dealing with such cases. References to these will also be found in our

analysis of the literature by Archambault and Fromm. Other than the above, the atrophy was not very remarkable. The right shoulder seemed higher than the left. There is spasm of the muscles of this shoulder. This is probably due to the fact that in addition to the maintaining of the weight of the right upper extremity against gravitational force, the incessant movements have produced the spastic condition in the muscles of this region. Not only are the limitation in gait and the muscular wasting of this patient important, but the reflex reactions of this individual among other positive findings, are also of particular interest. Of greatest interest is, however, the fact that this patient complains of pain in the affected extremity. This would indicate that there might be a lesion in the thalamus or that the fibres from the thalamus going to the caudate nucleus are affected, thus giving a combination of pain and athetosis. As we go along with our cases, the reader will see how reticent we are about making commitments regarding anatomical localizations. We cannot afford to be pounced upon by some outstanding clinician who would criticize our ability of localization.

There is a definite reflex inequality in this patient. The difference in the reflex reaction involved mostly the tendon reflexes of the right side as compared with those of the left side. In recent years some clinicians have stressed the role of tendon and other reflex reactions in clinical neurology. Although we have been much interested in this phase of the neurological examination, and particularly in facial and neck reflexes, since they reflect upon the seizure pattern, we omitted many reflex reactions from future cases because the fundamental physiology of the reflex mechanism is still shrouded in theory, and involves bioelectric concepts dealing with internuncials, rhythmic pulsations, reticular and other relay phenomena, etc., etc. The mechanisms of clonus and nystagmus depend, however, upon such theoretical concepts as shown by Lorente de No and Barany. For those neurologists who delight in such data, and in their possible relation to Muskens' myoclonic shock concepts, we have gone to the painstaking trouble of constructing our diagrams in such a way that the internal capsular and cortical reflex topography are shown in relation to the cytoarchitectonic and trigger zone areas of Foerster and Penfield. The right biceps, triceps, and radial reflexes are all four, whereas those of the similar reflexes on the left side are one, in magnitude. The right patellar and achilles are also four in reaction amplitude each, while the left patellar is two and the left achilles is one plus. The right abdominal is one in reaction magnitude, while the left is two; and the right Babinski is questionably positive, while the left one is negative. The findings in the reflex field suggest the existence of an involvement of the right or left caudate nucleus associated with a similar involvement possibly of the right or left thalamus. These furthermore point to the fact, as suggested by Tilney and Riley, that the caudate nucleus is responsible for the existence of athetosis. The presence of pyramidal tract involvement instead of the extrapyramidal, as seen in the positive Babinski sign, plus the fact that pain is felt in the affected extremity all would suggest that the caudate nucleus rather than the globus pallidus is affected. The association of fits and particularly

the presence of abdominal pain, with the possibility of motor and tonic disturbance in the gastrointestinal tract musculature makes the above case most interesting. The reader is therefore urged to refer not only to the caudate nucleus which would give him the background of the anatomical reasons for the athetosis, but also, to look up the anatomical details which we presented in complete form in previous pages referring to not only the cellular structure but also to the fibre connections of the anterior nucleus of the thalamus, near which is situated the head of the caudate nucleus. It might even be that the lesion in the case under consideration is located in neither of the above two structures themselves, but in the cortical fibre pathways leading to and from these bodies.

The cranial nerve examination of this patient was essentially negative. This included also fundoscopic examination. Sensory examination disclosed no reason for the complaint of pain in the right upper extremity. There was no evidence of hyperalgesia or hyperesthesia. The pain in that portion of the body was evidently due to some lesion of thalamic structures, of fibres from the cortex to the thalamus, or even to muscular strain caused by the incessant movements. It is a rather curious fact that individuals suffering from athetosis or Huntington's chorea seldom complain of pain in the parts which are in constant motion. Compression of the carotid sinus region gave negative results. Percussion of the liver area showed only a dulness of two fingers posteriorly. The gastrointestinal tract from the viewpoint of liver disorders and its relation to the extrapyramidal system in athetosis and other disturbances, has a longer history than one might suspect. The firmly established clinical syndrome of hepatolenticular degeneration stands out prominently along support of the above statement and as a possible reason for the leanings of Watts and Fulton in the direction of the extrapyramidal pathways from the cortex to the striatum, as the responsible routes mediating neurogenic gastrointestinal control. Such mediation does not eliminate the corticopontine and corticocerebellar pathways, since fibres from the corticostriate, pass by the way of the red nucleus to the pons and pontocerebellar system. Watts and Fulton were merely interested in the cerebral cortex in relation to the striatum and for this reason, stopped anatomically, at the latter structure. From the above it is evident, that cases showing extrapyramidal features, be they tremors, athetoses, ataxia, or facial masking, are of extreme importance especially if the aura definitely refers to gastrointestinal functional disturbances. The above data on this case, therefore merits a short analysis to prove a cerebral location of the lesion. If the reader takes upon himself to analyze the various problems which we touched upon in the presentation of the few facts dealing with the neurological examination, he will realize that we regretfully tore ourselves away from delving into the literature of the anterior nucleus of the thalamus and from that of the caudate nucleus. We also steered clear of involving ourselves in a discussion of the writings of Watts and Fulton to say nothing of those of Hare, Sheehan, Archambault and Fromm as well as in those of Muskens, Rosett and particularly Clarke and Davidson and Goodhart among various others. We might be accused by the neurologist of

not indulging in some worthwhile discussions. We feel rather guilty in the above respect and wish to state that we did so because we had overindulged in such dissertations and in the writings of the above authors on previous occasions. We could answer the above by stating that we would rather be accused of overemphasizing the literature on the gastrointestinal tract and at the same time not stopping and spending enough time on neurological descriptions, than if the opposite were true. We don't mind it if Wartenberg who has been so unmercifully taken to task by Archambault and Fromm, upon reviewing our data, finds that we have omitted something or other on muscular atrophy or even in the field of reflexes. We can promise him that in the presentation of cases later on, we shall make up for any deficiencies in discussions on muscular atrophy and even add a few regions of the body such as the pelvis, pudendal, intranasal and intraaural cavities which not only he omitted, but which even Archambault failed to refer to. We feel that this work is primarily for the sake of the gastroenterologist and not for the neuropsychiatrist. Later on, we might satisfy both of the above specialists by delving a little more into the literature dealing with the neuroanatomical background of the clinical findings. In the meantime we wish to make a few remarks in regard to the above case and its localization in the cerebrum (See Figs. 43-54, inclusive).

The chief feature in this case is the athetosis. This phenomenon of athetosis is not seen in spinal cord disease. It is seen in mesencephalic disease, but in that structure it is associated with paralysis of the third or fourth cranial nerves. Further down in the brain stem, it is also met with in various diseases of the pons. In this structure it is associated with paralysis of the facial nerve as well as with involvement of the sixth or abducent nerves. This patient does not have involvements of such nerves either on the same side of the athetosis and most certainly not on the opposite side. It is therefore neither a mesencephalic lesion nor a pontine which is operating in this case and causing the convulsions or the gastrointestinal disturbance, and surely not the athetosis. The only extracerebral portion of the brain which is left, is the medulla oblongata. Even in this structure, if athetosis is present, it is only associated with paralysis of the pharynx opposite to the athetosis or with a paralysis of the tongue or of the neck musculature opposite the paralyzed side of the body. What is therefore left is the cerebral hemisphere, and it is in this organ exclusively that we will find a lesion which would produce the combination of athetosis, convulsion and gastrointestinal disturbances. In the remaining cases of this group we expect the reader to apply the above method of differentiation for cases of athetosis, since we will not indulge in a detailed analysis such as the above because of the lack of space. Even for other syndrome groups, it might be well for the student to keep the above in mind. Although the syndrome of hepatolenticular degeneration points towards the striatum as being not unrelated to neurogenic control of gastrointestinal function, the mammillothalamic region seems to offer much more experimental evidence for such control than the former. The lenticular syndrome consists only

of one clinical entity and as such, might be ascribed to the striathalamic or thalamostriatal system of fibres which begin or terminate in the lenticular nucleus. We have previously emphasized the fact that with the presentation of cases in this pain syndrome group we intend to prove to the reader that all of our cases satisfy the main purpose of this communication, namely, that the neurogenic control of gastrointestinal aurae is essentially of cerebral and not mesencephalic, brain stem or spinal cord, and not even peripheral origin. We have illustrated the above by the presentation of two concrete cases. We shall continue to do so in the future by presenting more cases with many clinical findings. In the following few cases we intend to show the reader how to localize the lesion in the cerebrum when either the historical data is insufficient or when the neurological findings are meager, or both are defective (See Figs. 61, 66 and 67).

Case A. N. is a female 17 years of age who was admitted to the institution in December, 1926, complaining of epileptic attacks preceded by severe abdominal pain. The family history shows that her mother suffered from epileptic attacks which began when she was 21 years of age. Although the birth of the patient was natural and she weighed 7 lbs. at that time, her development was definitely delayed. She began to walk at 22 months of age and to talk at 30 months of age. The first epileptic attack occurred when she was 9 months of age. Most of the attacks are diurnal and of grand mal type. The greatest number of seizures in 24 hours was said to be four at the time of the admission, when she was also said to average about two attacks weekly for a four year period.

The admission record presented very little of positive neurological findings except that the patient was poorly developed. The family records and the early onset of the epilepsy therefore seem to place this patient as a case of hereditary or congenital epilepsy. The presence of grand mal attacks associated with gastrointestinal complaints, but particularly the existence of the former in the absence of cranial nerve paralysis situated opposite a paralysis of the extremities, would place the lesion responsible both for the epilepsy and the concomitant gastrointestinal disturbance in the cerebrum.

An item which is relevant in this patient is the fact that the convulsive attacks and the gastrointestinal complaints were not relieved by the administration of luminal, which was given for a number of years, as recorded in 1928, at ¾ of a grain daily, and in 1935 and for a number of years thereafter, when she was given 3 grains daily. Although we at times express ourselves in favor of phenobarbital therapy, it is unintentional for us to overstress it, since we feel that the ultimate cure lies along surgical lines. We are however interested in the special Eggleston-like, method of its administration. For a two year period one of us followed this method at the New York Polyclinic hospital beginning in 1938. Although the series of cases at that hospital was small, fair results were obtained at that time. Our method of graduated massive doses was at first marred by complications. We saw a case of coma associated with cerebral edema, in one of our series at the Welfare Clinic in New York. It was at this clinic where one

patient in whom this method was tried developed a peculiar psychotic syndrome characterized by a marked "witzelzucht". Eventually she recovered. We resumed our studies of these cases in the postbellum period. It is rather unfortunate that our method does not lend itself to be followed in institutional cases, since brain tumor cases would be harmed by operative delay and the personnel seems inadequate for tumor differentiation from epilepsy. The records of this case show that from the year 1927 until the year 1938 inclusive, the patient had a total of 1,506 epileptic attacks. Of these, only 207 were reported as petit mal. In other words, the remaining 1,299 attacks were of the grand mal variety. We have previously given the reasons why we believe that the petit mal attacks were usually greater than the number recorded. From 1927 until 1932 covering each year, the patient had 88, 186, 99, 146, 114, and finally 72 attacks per year respectively. From 1933 through 1938 the patient had 145, 188, 156, 90, 129, and finally 191, per year respectively beginning with the year 1933 and terminating in the year 1938. The above data is offered to show how frequent and severe must be the strain upon the gastrointestinal tract resulting from recurrent epileptic attacks and their associated aurae. We feel that the petit mal seizures are usually many times the number of the grand mal type. Considering the above there must be an unusual upset in the secretory and muscular state of the gastrointestinal tube. This would agree with the reports in the literature offered by Lennox and Cobb. In all future cases where the seizure record is offered it is essential that the reader keep the above data in mind and that he refer back to the actual facts as presented by Lennox and Cobb (See Fig. 65).

Although we were interested in stressing the importance of seizure frequency and time of occurrence as well as the type of attack, what interested us most in the above case was the familial and possible congenital features. In our analysis of the 300 cases to illustrate the methods of taking a history, we specifically emphasized the taking of a hereditary history. In our procedure with the above we were successful in going back a number of generations. In the above case however, we only have a single item to guide us, that is the maternal history. This alone is however sufficient, since the onset of the epilepsy in the mother was at such an advanced age when organic disease such as syphilis or tuberculosis are the likely causes of epilepsy. Sometimes trauma will cause epilepsy, in an adult and in the course of pregnancy of such a patient, a number of attacks will occur, one of which will be sufficient to produce injury to the fetus also resulting in epilepsy in the new born, or of a hemiplegia which is congenital and an epilepsy which ensues even a number of years after birth.

Every item in the case history, no matter how seemingly insignificant, is therefore, of importance. Of greater importance is sometimes the fact that no positive neurological findings were recorded at the time of the examination. This is seen in the case of C. F. an adult male 20 years of age who was studied because of his aura of severe abdominal pain associated with nausea. The patient also

suffered from grand mal attacks which began soon after his fall from a chair at 6 months of age.

The neurological examination was essentially negative except that there were some changes in the outline of the discs on fundoscopic examination. This case is therefore one in which the cerebrum is involved by some scarring or some other process. The absence of hemiplegia with contralateral cranial nerve findings, definitely places the lesion responsible for the convulsions and for the abdominal pain in the cerebrum, as against the mesencephalon, pons or other parts of the hindbrain. The following case is another example in which there are few findings for the examiner to make a definite localizing diagnosis. Yet, in spite of that, because of the existence of grand mal seizures associated with abdominal pain, we are forced to place the lesion in the cerebrum. It is true that some authorities believe that the mesencephalon contains centers for the origin of convulsions. One does not need a Benedict-Weber Syndrome as an indication of a mesencephalic lesion. Such convulsions are supposed to have a specific pattern and have been described as consisting of such, in which the eyes look toward the hemiplegic side.

G. L. is an adult female who was admitted to the institution suffering from grand mal fits both of the nocturnal and diurnal variety which are invariably preceded by pain in the stomach. The patient is too deteriorated to give a detailed history of her attacks. She is also incapable of describing her symptoms of the gastrointestinal or other types, as will be seen in the presentation of data. Neurological examination finds a patient who is only partially cooperative so that she carries out minor orders which indicate that her gait is not ataxic and that she does not suffer from an unusual dysmetria. She also presents no definite evidence of extensive paralysis. Her motor and muscle strength are not appreciably affected. Her movements are rather peculiar. She sits with her hands and legs crossed and only rarely evidences signs of spontaneous movement. When she smiles, the right side of the face seems to be partially paralyzed. There is also a narrowing of the right palpebral fissure. We are not aware of any description in the literature of a supramesencephalic Horner's syndrome. The Horner's syndrome of the brain stem also needs clarification. In all of our publications on the neurology of epilepsy we have had the urge to describe various types of cerebral Horner's syndromes in our cases, but as with our reticence with myotatic reflexes in these cases, we feared the criticism of outstanding clinical neurologists. We thought that we would be made guilty of clogging the wheels of neurologic progress by introducing items into an already overburdened nosologic literature. If such attempts will interfere with the publication of papers on new drugs in epilepsy or other therapeutic attempts for the immediate relieving of the sufferings of the epileptic patient, we are willing to postpone the recording of our observations of definite indisputable factual entities. In addition to the above, her right nipple is larger than the left one and she suffers from a right lower dorsal scoliosis. Examination of the eye grounds shows an optic atrophy. From

the above findings it becomes evident that the patient is suffering from a cerebral lesion because of the emotional facial paralysis and the mental changes in addition to the convulsive syndrome.

These signs of neurosomatic deterioration are associated with evidences of involvement of the optic thalamus as seen in the paralysis of emotional expression. It is difficult to speculate as to whether the gastrointestinal aura preceding the epileptic spells and the paralysis of emotional expressions are the result of injury to the anterior nucleus of the optic thalamus and subsequent degeneration along the mammillothalamic tract. It may even be that the trouble originated in the cerebral cortex of the frontal lobe which is also a center for both the functions presented above. We know from the writings of Watts and Fulton that gastrointestinal disturbances occur as a result of stimulation of the premotor cerebral cortex. We also know from the writings of Tilney and Riley and others, that feeling tone is also localized in the cerebral cortex of the frontal lobe. The above few facts give us a clue into the vastness of pathologic changes that one might encounter in this, so-called simple phenomenon of neurosomatic deterioration, whether it starts with disturbances of centers controlling emotional expression or otherwise. We are, however, at present especially concerned with elaborating upon such neurological syndromes.

We are merely anxious to establish the existence of a lesion in the cerebrum in cases of patients who suffer from convulsions whose fits are preceded by the phenomenon of abdominal pain. The above patient presents both of these symptoms and also shows definite evidence that the cerebrum is involved, and that there is no substantial affection of the mesencephalon, the pons, and the medulla oblongata except possibly in the form of descending degeneration. Examination of the centers of localization of the epileptic fit, as seen in Fig. 55, furthermore indicates that grand mal attacks occur mainly as a result of injury to the cerebrum. The above patient presented no other findings except variation in blood pressure, the right side giving 110 over 60 with the left side having a systolic of 90 and diastolic of 60.

In the remaining cases of this syndrome of abdominal pain aura, we shall present detailed data dealing with each case and reserve extensive comments until the end. Some of the cases to be presented show detailed records of observation of frequency of fits in addition to a complete past personal history as well as substantial neurological findings. In one of the cases, pneumoencephalographic findings are added to the neurological examination and even the record of a subdural operative procedure is discussed. Our interests at present are not in detailed presentation of such technics. We are mainly concerned in proving to the reader that when a patient suffers from convulsive fits that are preceded by symptoms pointing towards involvement of function of the gastrointestinal tract manifested by preparoxysmal pain, that there is damage to the cerebrum and probably to certain tracts that connect with the mammillothalamic system or the spinothalamic pathways, and in this way, the corticodiencephalic or diencephalocortical centers

are affected. We are as yet not even concerned with proving the existence of specific involvement of the mammillary or spinothalamic structures. We merely want to impress the importance of establishing the fact that when vomiting or abdominal pain or some other gastrointestinal syndrome is present in a patient who presents definite neurological clinical signs, that the seat of the trouble is not in the vegetative centers in the brain stem, or of those in the spinal cord, provided the patient presenting such symptoms suffers also from convulsions. By the above statements we do not wish to imply that pressure upon the brain stem could not produce symptoms of vomiting associated with convulsions in a patient who is suffering from a brain tumor which presses upon the lower regions. It may even be that in most cases of cerebral neoplasm, a combination of the above mechanism really operates in producing both the vomiting and the convulsion. It has been fairly well established however, that the clonic phase of the convulsion is due exclusively to cerebral stimulation. We are therefore correct in assuming that in the average type of seizure consisting of clonic as well as tonic components, there must be cerebral involvement and that pressure upon the so-called "vital centers" in the brain stem would be insufficient for the production of the complete picture.

Patient S. S., an adult female, 25 years of age, was admitted to the institution complaining of an aura of abdominal pain situated on the left side of her abdomen in addition to grand mal convulsive attacks. Her epilepsy, as well as the gastrointestinal symptoms were of twenty-three and a half years duration at the time. When she was admitted to the institution in 1928 it was found that her family history was essentially negative for nervous trouble. Her mother died at the age of 45 years of a liver operation. The patient's past history showed that her delivery was natural and that she weighed nine lbs. at the time of her birth. She was breast fed and her teething was normal. Her development appears to have been uneventful. She began to walk and talk at one year of age and she entered school at the age of 5 years.

Her epileptic attacks were of the diurnal and nocturnal variety of the grand mal character and occurred more during the day than at night. The greatest number of fits that ever occurred in one day, was six. The convulsions seem to be more frequent in the last few years. These seem to be uncontrollable with a grain and a half of phenobarbital daily.

The neurological examination showed a patient who presented some limitation in automatic associated movements in walking. Motor ability appeared to be normal throughout. The patient was however not cooperative enough to carry out intricate movements involved in the testing for dysmetria, adiadochokinesis or past-pointing. There was a definite atrophy of the right side of her chest. The tendon reflexes were greater on the left side than on the right, particularly her left triceps, and achilles. Her abdominal reflexes were absent, but otherwise, there was no definite evidence of pathological reflex involvement. Although we have already remarked about our reticence in dealing with the much involved theories of the mechanism of reflex reactions, the relationship between the scratch

reflex and alternating or rhythmic reflexes and the mechanism of clonus, and of myoclonic reactions as proposed by Barany, Lorente de No and Muskens, seem to lure us, since they reflect upon the problem as to whether the tonic intestinal responses should be classed under the heading of motor phenomena as per Watts and Fulton, or placed in the category of reflexes. If we resort to the latter concept, then the mechanism of reciprocal innervation which Watts and Fulton were so hesitant in putting their stamp upon in so far as they might apply to the results of their experiments upon cortical ablation and irritation, becomes a matter which is easily explained on the basis of the work on nystagmus and the vestibuloocular reflex arc by R. Lorente de No. The last author recognizes reciprocal innervation principles, but explains them on the basis of a passive inhibition resulting from fatigue of cell groups operating in chains of rhythmic reflexes. Many such chains are present in the mammillothalamic system. The examination of the eye grounds showed a definite blurring of the upper disc margins and this was more marked on the right than on the left side. Her left pupil was slightly smaller than the right one. There was also a slight narrowing of the posterior part of the tongue. Her face showed a definite fixity characteristic of the neurosomatic facies, approaching almost that seen in Parkinsonism.

Although this patient presents no definite extensive paralysis of one side of the body, the findings of atrophy as well as reflex changes and cranial nerve involvement associated with grand mal seizures, definitely points to the fact that the cerebrum is affected in this case. The definite delay in development of this individual as seen in her mental backwardness, also points towards a cerebral affection, instead of involvement of the brain stem, spinal cord, or peripheral nerves. Particularly in the last two mentioned types of structures do we seldom find convulsive reactions, although gastrointestinal symptoms might be present. We refer to such congenital diseases as Friedreich's disease or other forms of spinal diseases that are exclusively such, and in which there is no lesion of other portions of the nervous system, that might cause convulsions.

Another interesting feature which this patient presented, was the persistence of urinary reactions in association with the gastrointestinal symptom and with the convulsions. It may be that some patients urinate during convulsive attacks, because of fullness of the bladder. When urination invariably occurs with every epileptic attack, and does so over a period of many years, it stands to reason that there might be some involvement of the centers within the cerebrum which control urination, in the same way as are implicated such centers that control vomiting, nausea, and so forth. From 1929 until 1939 this patient suffered from 557 seizures, or an average of 55 attacks a year. The petit mal attacks were recorded to occur less frequently than the grand mal variety. Aside from impressing the reader with the fact that the above patient's lesion which produced the gastrointestinal aura as well as the convulsions, was located in the cerebral hemisphere, we could have presented symptoms other than those of the neurological findings to substantiate our conclusions. We have for instance, shown that the delay in the

mental development of this patient, also proved that the disease affecting her was located in the cerebrum. Another very important point to be stressed in this case is the fact, that, in addition to suffering from abdominal pain before a spell this patient usually becomes mentally disturbed and fights with other patients. Prior to her convulsions she always says that her people are calling her on the phone. She therefore has definite auditory hallucinations. Such phenomena, particularly when related to epileptic attacks, indicate that there is, not only an involvement of the cerebrum, but that a special lobe such as the temporal portion of the aforementioned structure is specifically involved. It may be, however, that the temporal lobe is not the only one that is responsible for the auditory hallucinations. One of the geniculates, which is a part of the thalamus, might be the seat responsible for the auditory phenomena. We could, if we had the space, continue to elaborate in detail as we did above, about each patient, but we feel at present it is important that the reader be impressed with the fact that the portion of the nervous system which is mostly responsible for gastrointestinal disturbances when they precede or follow epileptic attacks is usually the cerebrum.

What has been said above with regard to aurae which consist of sensory gastrointestinal symptoms might also be applied to urinary symptoms which occur before, during, or even after the epileptic attacks. Particularly in the above case we could have elaborated more on the urinary reactions, since they invariably accompany almost every epileptic spell in this patient. We have no time, however, to stress them at present, and refer the reader to Fig. 5 which deals with cerebral control of urination as shown in the work of Marburg and Czyhlarz, Kleist, Foerster, Stewart and last but not least, Frazier, Watts and Uhle.

In the following case it will not be necessary to stress the fact that in a patient who suffers from convulsions as well as from a gastrointestinal aura the lesion is situated in the cerebral hemisphere exclusively. The paralysis contralateral to the lesion as well as the absence of ability to appreciate sensory stimulation on one side of the body definitely points towards the cerebral hemisphere and excludes involvement of the brain stem, spinal cord, and peripheral nerves.

S. B. was 22 years of age at the time that he was studied. When he was admitted to the institution, the chief complaint consisted of convulsive spells that were preceded by an aura, which consisted largely of abdominal pain. Careful interrogation shows that the aura is not a very simple one. The patient claims that a cloud comes over his eyes before a spell and that, in addition to pain in the "stomach", he gets nervous and feels as if something is turning over inside of him, in the region of the epigastrium and in the navel, so that he brings up a great deal of gas, and sometimes becomes nauseous and vomits. He also claims that he suffers from a nervous feeling in his epigastrium and feels like having a spell with almost every meal; but for some unknown reason, these spells are merely threatened, but never really occur with every meal. His past personal history seems irrelevant except that his spells came on him when he was one year

of age. This is rather early in life and is not infrequently suggestive of a birth injury, intrauterine disease, or congenital and developmental brain defect.

Neurological examination shows that he suffers from a left hemiplegia. It is more a monoplegia of his left upper extremity which is held in flexion while he is walking. Tests for motion show that the patient is able to raise both of his arms, but that the left one is held in partial elevation with a peculiar position of the fingers. There is a definite paralysis of extension of the left hand and forearm. Coordinative tests show that diadochokinesis is normal, except that the hand is held in flexion during the execution of such movements. The finger to nose test is carried out well and so is the finger to finger test. Muscle strength tests show that there is weakness on extension of the left hand, the wrist and fingers included. The existence of paralysis in one extremity points toward the involvement of the cerebrum since it is commonly known that a paralysis which is due to a lesion in the mesencephalon, such as is seen in the Benedict-Weber syndrome is always a complete, one sided one. It is common knowledge that cortical lesions invariably produce a monoplegia instead of a hemiplegia. What has been said above for the mesencephalon is also true for a hemiplegia which is due to a lesion in the pons or medulla oblongata. In syndromes such as those of Foville, Millard-Gubler, Raymond-Cestan, Avellis, Schmidt, and Jackson and in numerous others in which there is inability to move one side of the body associated with homolateral cranial nerve disturbances, the paralysis is always complete. In some of the above mentioned syndromes there is a complete hemiataxia, hemichorea, or hemitremor instead of the hemiparesis. Whenever such syndromes (excepting those with isolated glossoplegia, pharyngoplegia or accessory nerve paralysis) consist of extremity involvement, they, as a rule, affect both the upper and lower extremities as well, except in special cases of thrombosis of branches of the basilar artery. This is likewise true for involvements of the internal capsule of the cerebrum. In our patient we find, however, that the paralysis involves only one of the extremities. Such a paralysis can therefore not be present as a result of a lesion in the brain stem nor of the internal capsule, but must involve the cerebral cortex. From the presentation of the above data it becomes evident that the condition responsible for the patient's epileptic attacks as well as for his gastrointestinal symptoms ought to be located in the cerebral hemisphere and is probably involving part of the cerebral cortex.

The above would be true even if this patient presented no other positive neurological findings. This is, however, not the case, as we see from the following additional positive neurological symptoms and signs which this patient shows. There is a definite atrophy of the left foot and a marked wasting of the left forearm, hand, and arm. There is also a definite atrophy of the left sternocleidomastoid muscle. The above atrophy classes this patient into the group of total hemiatrophy. The above clinical phenomenon of total hemiatrophy is interesting from the standpoint of the detailed presentation of the literature on this subject as stressed in our quotations of Archambault and Fromm. The reader is referred to

the previous pages on this subject since it will help him to determine the factors involved in the anatomical localization of the lesion responsible for the wasting as seen in the above patient. The reader is furthermore urged to refer to Fig. 39 which deals with the entire subject of total hemiatrophy. In all of our joint publications on the neurological findings of epileptics, we invariably referred to the hemiatrophic, monoatrophic, or group atrophy of selected muscular, glandular, chondral or osseous structures or viscera. We invariably felt that some of the tendencies toward pulmonary diseases or gastrointestinal disease might be due to regional atrophy or hypogenesis. We very seldom expressed ourselves elaborately along such lines, for instance, by blaming menstrual upsets occurring previous to seizures as being epileptogenic. We feared that such ideas would be unacceptable in a neurologic literature which paid scant attention to or failed to emphasize similar findings by such neurologic luminaries as Muskens, Gowers, Brown-Sequard, William G. Spiller, etc., etc. Although the literature points to involvement of the aqueduct of Sylvius primarily, and to other parts of the brain, particularly around the third ventricle in cases of total hemiatrophy, we do not agree with this in our cases. The reason for our insistence upon exclusive cerebral involvement in this case in particular, and in all of our cases of epilepsy, is the fact that generalized clonic combined with tonic convulsions always mean that the cerebrum is the offending portion of the encephalon. In regard to the above, one can always say that in the brain of a patient such as one with whom we are dealing, one does not necessarily have to infer that a lesion which is situated in the cerebrum and which produces paralysis and convulsions as well as gastrointestinal symptoms, in order to produce wasting of the body, must also be localized in the cerebrum. It could be so localized, but such a lesion producing muscular wasting could also extend into the mesencephalon. Furthermore, the trophic disturbance is merely a concomitant sign which may be present in patients who do not have convulsive symptoms and whose convulsive symptoms, if present, are not necessarily preceded by gastrointestinal symptoms. In other words, it would be well for the present, to caution the reader against concluding that the authors assume that those pathways which control trophic phenomena are identical with those responsible for the neurogenic control of gastrointestinal operations. Although the above is true and we could pursue various other types of neuroanatomical differential diagnostic discussions, we feel that at present all we are interested in is that the neurological findings in most cases who suffer from convulsions that are associated with gastrointestinal aurae, point towards affection of the cerebral hemisphere exclusive of all other structures of the central nervous system. We prefer to emphasize this when dealing with the clinical material in this syndrome group, no matter what other relevant and striking features come into view. Although we have attempted to confine our attention to presenting the positive neurological findings of our cases, we are at times diverted into discussions and reference to the above. In the syndrome of abdominal pain, even though we seem to be rather technical along the lines of clinical neurological topics, these are

merely presented with one point in mind, namely, to show that the material is relevant and conclusive, pointing towards the cerebrogenic control of gastrointestinal operations.

The reflex examination of this patient shows that the reactions of the left side of the body are exaggerated as compared with those on the right. Besides the above, there is also an absence of the right cremasteric reflex. We are again impelled to refer to reflex concepts since they have been construed as being related to the mechanism of tonus which seems to be highly organized in diencephalic structures. It is particularly in such structures in which R. Lorente de No and many others pointed to the existence of short axone neurones and cell aggregations that preside over the operations of rhythmic reflexes, alternating reflexes and influence even the scratch reflex responses. Tonus, whether of the smooth or skeletal muscle variety is a factor in reflex responses. Even though gastrointestinal tonic responses are affected in a patient whose hemihypertonicity is accompanied by trophic and reflex phenomena in the skeletal muscles, we do not intend to imply a fundamental relation between skeletal muscle reflex responses and those of the gastrointestinal tract. Watts and Fulton, Spiegel, and others, pointed to such relationships, but they did so mostly, on the basis of the results of laboratory experiments, pointing to no more than one, or two, clinical examples. There is, in addition, an exaggeration of the left scapular reflex region and tapping the right side of the face produces a bilateral mass response. One of us (Weingrow) has observed the above type of response as well as other types of reflex responses which were described by him in the literature from 1931 until 1937. Reactions such as the above and similar ones, although very interesting, have as yet not been accepted and incorporated into the average text book on epilepsy or otherwise. We will therefore not stress these and similar reflex reactions, although these might at times be extremely serviceable in establishing the localization of a lesion. Brown-Sequard, Riddoch, and others have referred to similar responses which we also mentioned in our previous joint publications.

In addition to the motor, trophic, and reflex disturbances in this case there were also definite positive sensory findings. The entire left side of the body of this patient presented a definite diminution in perception of touch, vibration, temperature and pain. This decreased ability to appreciate sensation, involved the left upper and lower extremities but the left side of the face was definitely excluded. This was not the case in the trophic disturbances, since the sternomastoid was also affected on the left side. Aside from the above findings there was nothing to contradict the conclusions at which we arrived, with regard to localization. There was a slight facial asymmetry. There was also a marked lateral nystagmus on looking to the right. This is rather important especially with reference to exact localization of the lesion in the direction of the extrapyramidal pathways of the cerebrum and probably those of the corticocerebellar tracts in the frontal lobe. This finding might point to involvement of frontopontine fibre systems. In our

discussion of other syndromes we shall dwell in detail upon the corticocerebellar pathways in relation to gastrointestinal neurogenic control.

Examination of the fundi of this patient shows a marked optic atrophy. The choroid was very much accentuated in the lower left quarter at the margin. This is probably due to changes in the region where the meninges fold over the optic nerve which they accompany through the optic foramen, and extend to the back of the eyeball. The nerve head of the right fundus was smaller than that of the left one and there was a marked disc blurring; the areas about the vessel structures being rather cloudy. The carotid sinus region of this patient was stimulated but no convulsive reaction was elicited. There was however definite evidence of contraction of the area of liver dulness and flatness in this case since this area measured four fingers anteriorly and three fingers posteriorly. In patients who present extensive muscular, osseous or chondral atrophy it should not be surprising that the liver might also show hypogenetic degenerative changes. These degenerative changes need not be on a gastrointestinal neurogenic basis but independent of the same. In association with the degenerative changes in the thalamus, we would therefore have a hepatothalamic descending degenerative disease syndrome in the same way as we have a hepatolenticular degenerative disease (Wilson's Disease). We might also have a hepatocaudate degeneration. There is no reason why we should not have a hepatoputamenal degenerative extrapyramidal neurosomatic syndrome. If we are not mistaken, there is a quite extensive literature pointing to the existence of some of the above syndrome combinations. On the basis of the foregoing, and particularly on the experimental evidence of Watts and Fulton, we could expect many types of hepatocerebral descending degenerative disease combinations not unlike the syndrome of Wilson. We shall present evidence in future cases to prove our point. We shall and must desist from naming such syndromes because of the stigma attached to the burdening of the literature with names, without adding facts of diagnostic or substantial therapeutic significance.

The case of the above patient is therefore clear. The localization is definitely proven to be in the cerebrum. We have shown that there are areas within the cerebrum, particularly in the region of the corticodiencephalic system, which control symptoms referring to the gastrointestinal tract, and that such symptoms are not only sensory consisting of pain but also motor consisting of nausea as well as vomiting together with the gastralgic and enteralgic complaint. In the above case, as well as in a few of the preceding ones, there was clinical neurological evidence of definite localizable lesions in the cerebrum which were shown to be productive not only of the convulsions but also of the gastrointestinal aurae consisting of abdominal pain as well. In the remaining cases of this syndrome of abdominal pain we might be unable to point to isolated lesions similar to those presented in some of the above cases. There will, however, be definite evidence that the cerebral hemispheres contain pathologic changes which will be shown to be diffuse in some instances and rather extensive but local in others. Part of the brain injuries will

be responsible not only for the convulsions, but definitely for the gastrointestinal symptoms and even for the paroxysmal and nonparoxysmal mental disturbances. With the above and the subsequent cases in this group syndrome of abdominal pain we are confident that we can definitely prove to the reader that the seat of the trouble responsible for abdominal pain as a symptom either occurring with grand mal, petit mal or independently thereof is located in the cerebrum exclusively and nowhere else in the other parts of the central nervous system consisting of the mesencephalon, metencephalon, spinal cord or peripheral structures.

Eventually when we will deal with other gastrointestinal syndromes we shall employ the same method of logical exclusion of anatomical structures and show that the neurogenic control of the gastrointestinal system might be narrowed down to the mammillothalamic, preopticomammillomesencephalic system, or that gastrointestinal function is directed by the spinothalamic or some other system which is connected with the corticodiencephalic and diencephalocortical cerebral pathways.

From time to time we propose to deviate from pure anatomical discussions such as the above, even though they tend to fortify our stand and offer extensive material in support of the same by the literature. Our deviations will be to show that gastrointestinal symptoms are not invariably due to pressure such as is met with in cases of brain tumor or by toxic influences such as is seen in the vomiting of fevers, diabetic coma, uremia, etc., but to fibre path stimulation.

(*To be continued*)

CHAPTER ACTIVITIES

Boston Chapter

The Boston Chapter of the National Gastroenterological Association will meet on 16 November 1950 at the Carney Hospital in South Boston, Mass., at 8 p.m.

A symposium on "Ulcerative Colitis" will be held, with Dr. Emanuel Deutsch, Instructor in Medicine, Tufts Medical School, presenting the medical aspects; Dr. Timothy Francis, Assistant Professor of Surgery, Tufts Medical School, the surgical aspects, and Dr. Norris Butler Flanagan, Instructor in Psychiatry at Tufts, the psychiatric aspects.

Dr. William E. Browne, Clinical Professor of Surgery at Tufts, will present a paper, "Nutritional Disturbances in Surgery".

New Jersey Chapter

The New Jersey Chapter of the National Gastroenterological Association met on 30 October 1950, at the Academy of Medicine of Northern New Jersey in Newark.

Dr. Leo Siegel of Newark presented a talk on "Dsyphagia Lusoria" during the scientific session.

Dr. Julius Gerendasy was unanimously elected to the Executive Council. The members present discussed a symposium on a gastroenterological subject to be given some afternoon, and Dr. Andrew J. V. Klein, chairman of the program committee, was appointed to look into the matter and report on it.

New York Chapter

The New York Chapter will meet at the New York Academy of Medicine on 13 November 1950.

Papers will be presented by Dr. Richard H. Marshak, Adjunct Radiologist, Mount Sinai Hospital, on "Roentgen Features of Ileojejunitis", to be discussed by Dr. B. B. Crohn; Dr. A. Goldschmidt, on "Multiple Polypi of the Colon in Old Age", discussed by Dr. L. J. Druckerman; and Dr. Henry J. Janowitz, Gastroenterology Research Laboratory, Mount Sinai Hospital, to be discussed by Dr. Anthony M. Kasich.

Members of the medical profession are cordially invited.

NEWS NOTES

1951 Prize Award Contest

The National Gastroenterological Association again takes pleasure in announcing its Annual Cash Prize Award Contest for 1951. One hundred dollars and a Certificate of Merit will be given for the best unpublished contribution on Gastroenterology or allied subjects. Certificates will also be awarded those physicians whose contributions are deemed worthy.

Contestants residing in the United States must be members in good standing of the American Medical Association. Those residing in foreign countries must be members of a similar organization in their own country. The winning contributions will be selected by a board of impartial judges and the award is to be made at the Annual Banquet of the National Gastroenterological Association in September of 1951.

Certificates awarded to other physicians will be mailed to them. The decision of the judges will be final. The Association reserves the exclusive right of publishing the winning contribution, and those receiving certificates of merit, in its official publication, The Review of Gastroenterology.

All entries for the 1951 prize should be limited to 5,000 words, be typewritten in English, prepared in manuscript form, submitted in five copies, accompanied by an entry letter, and must be received not later than 1 June 1951. Entries should be addressed to the National Gastroenterological Association, 1819 Broadway, New York 23, N. Y.

Fifteenth Annual Convention

An interesting scientific program, presented by capable speakers, made the Fifteenth Annual Convention of the National Gastroenterological Association, held at the Hotel Statler in New York City on 9, 10, 11 October 1950, an admirable success.

Colorful, informative scientific and commercial exhibits were on display during the convention, attracting a great many visitors.

Much of the success for the outstanding convention resulted from the efforts of the program committee, consisting of Dr. Anthony Bassler, New York, N. Y., chairman; Dr. William Reid Morrison, Boston, Mass.; Dr. Roy Upham, New York, N. Y., and Dr. Samuel Weiss, New York, N. Y.

Proceedings of the convention will be published in The Review of Gastroenterology during 1951.

Convocation Ceremony

One of the most outstanding impressive features of the convention was the cap and gown Convocation Ceremony held at the Hotel Statler, on Monday afternoon, 9 October 1950, at 5 p.m. One hundred twenty-three Members, Associate Fellows, Fellows and Honorary Fellows received their certificates at this ceremony.

Those receiving Honorary Fellowship certificates were Dr. G. Randolph Manning, New York, N. Y., first president of the Association and for many years its able secretary; Dr. Frank C. Yeomans, Great Neck, N. Y., a charter member of the Association and a member of its Executive Board, and chairman of the membership committee for many years, and, in absentia, Alfred Edward, Baron Webb-Johnson, of London, England, former president of the Royal College of Surgeons, who participated in our course and convention in Boston in 1949.

The address of welcome was delivered by Dr. Kenneth M. Lewis, president of the Medical Society of the County of New York, and the music was furnished by Dave Tarras and his orchestra, through the courtesy of our treasurer, Dr. Elihu Katz.

Rev. Henry C. Offerman, pastor of Christ Lutheran Church, New York City, delivered the invocation, and Rabbi O. Asher Reichel, of the West Side Institutional Synagogue of New York City, delivered the benediction.

Dr. C. J. Tidmarsh, Montreal, Canada, President-elect of the Association, presided, and certificates were presented by Dr. H. W. Soper of St. Louis, Mo., president.

A picture of part of the group, taken before the ceremony, appears elsewhere in this issue.

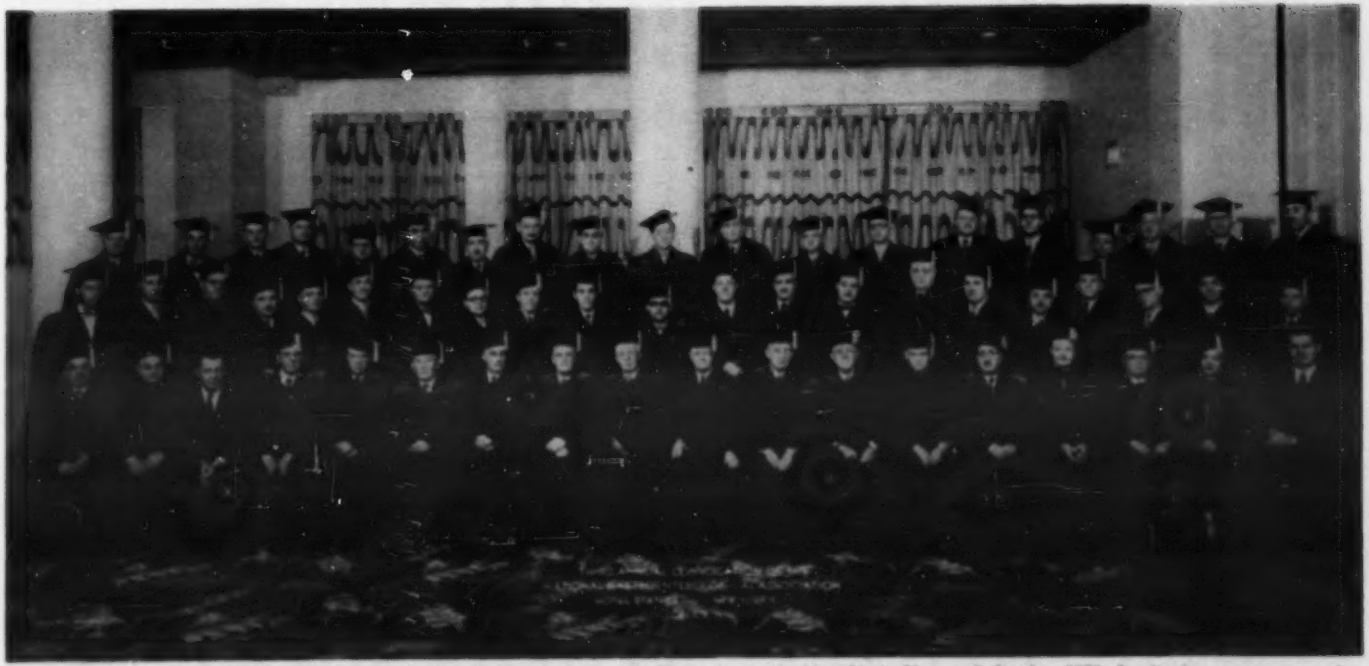
President's Reception

The president's annual reception was held after the Convocation Ceremony on Monday, 9 October 1950 at the Hotel Statler in New York City, and was again made possible through the kind cooperation of Winthrop-Stearns, Inc. Members of the Association and guests were invited to attend.

Annual Banquet

On Tuesday evening of the convention week, members of the Association met for their annual banquet at the Hotel Statler. Dr. Roy Upham, Secretary-General of the Association, was toastmaster. At the banquet, Dr. C. J. Tidmarsh, Montreal, Canada, assumed the presidency of the National Gastroenterological Association.

The judges for the 1950 Prize Award Contest reported that they regretted to advise that none of the entries had achieved the standards necessary to merit the award, and consequently no prize was given for 1950.



Part of the group who participated in the Third Annual Convocation at the Hotel Statler in New York City on 9 October 1950. In the first row are, starting with the third from the left, Rev. H. C. Offerman, Dr. Harry M. Eberhard, Dr. Frank C. Yeomans, Dr. G. Randolph Manning, Dr. William W. Lermann, Dr. C. J. Tidmarsh, Dr. Anthony Bassler, Dr. Horace W. Soper, Dr. Kenneth M. Lewis, Dr. Roy Upham, Dr. Sigurd W. Johnsen, Dr. William C. Jacobson, Dr. F. H. Voss, Dr. Samuel Weiss, and on the extreme right, Rabbi O. Asher Reichel.

6401

Postgraduate Course

Three days of convention activity of the National Gastroenterological Association were followed by three days of medical information and instruction at the course in Postgraduate Gastroenterology.

Directed, as last year, by Dr. Owen H. Wangensteen, Minneapolis, Minn., who served as surgical coordinator, the course received added impetus through the associate directorship of Dr. I. Snapper, New York, N. Y., who was medical coordinator.

In addition to Drs. Wangensteen and Snapper, there were 33 other officers of instruction drawn from the medical schools in New York City and vicinity, whose presentations were of extreme interest to those who took the course.

A banquet for those attending the course, and a reception to Dr. Wangensteen, were held on Friday evening, 13 October 1950, at the Hotel Statler.

The papers presented at the course and the discussions and questions and answers from the floor will be published during 1951 in The Review of Gastroenterology.

Annual Meeting of the National Council

The annual meeting of the National Council of the National Gastroenterological Association was held at the Hotel Statler in New York City, on Sunday afternoon, 8 October 1950, with Dr. Roy Upham, Secretary-General, presiding.

After reports from various chapter representatives, the council proceeded to the reelection of the following members of the Executive Board for a period of four years: Dr. Harry M. Eberhard, Philadelphia, Pa.; Dr. C. J. Tidmarsh, Montreal, Canada; Dr. Benjamin F. Bernstein, Brooklyn, N. Y.; Dr. William W. Lermann, Pittsburgh, Pa.

The name of Dr. Owen H. Wangensteen, Chairman of the Department of Surgery, and Professor of Surgery at the University of Minnesota Medical School, and for the past two years the director of our course in Postgraduate Gastroenterology, was presented to the Council for election as Honorary Fellow, and upon motion duly made, seconded, and carried, Dr. Wangensteen was unanimously elected Honorary Fellow.

Dr. Hyman I. Goldstein, Historian of the Association and a delegate from the New Jersey chapter, then proposed a rising vote of thanks to Dr. Roy Upham, Secretary-General of the Council, for his capable management of the Council meetings and chapter affairs for these many years. The rising vote of thanks was unanimously carried.

In view of the fact that a new constitution was to be adopted at the annual meeting of the Association on the following day, the meeting of the National Council adjourned *sine die*.

Annual Meeting of the National Executive Board

The annual meeting of the Executive Board of the National Gastroenterological Association was held at the Hotel Statler in New York City, on Sunday afternoon, 8 October 1950.

The Secretary-General, Dr. Roy Upham, reported that the Council had the previous day elected four of its members to the Executive Board for a term of four years.

The New York and San Francisco chapters presented for ratification the applications for membership of the following, which applications were accepted as indicated: Dr. Sidney M. Barth, Brooklyn, N. Y., Member; Dr. Claudius Y. Gates, San Francisco, Calif., Fellow.

It was agreed, that in view of the pending adoption of the new constitution on the next day, the election of officers be tabled until the new constitution had been adopted.

It was unanimously voted to approve the rental of larger office quarters as recommended by the committee, and the committee was instructed to negotiate further, and have the lease drawn for the premises.

A decision on the meeting place for the 1953 convention was tabled, pending the meeting of the newly-constituted Executive Committee.

Annual Meeting of the National Gastroenterological Association

The annual meeting of the National Gastroenterological Association was held at the Hotel Statler in New York City on Monday, 9 October 1950.

Reports on the status of the membership, The Review of Gastroenterology, the program and the treasury, the work of the research committee, and other committees, were made by the various committee chairmen. The chairman of the constitutional revision committee, then advised those assembled that the proposed draft of the new Constitution and By-laws had been forwarded to each member for their consideration prior to the meeting. He further stated that the draft had been thoroughly discussed and approved by the Executive Board, and recommended that the Constitution and By-laws as drafted be approved by the Convention.

Upon motion duly made, seconded, and carried, the new Constitution and By-laws were adopted to take effect immediately.

Under the provisions of the new constitution, the election of officers was to take place at the annual meeting of the National Gastroenterological Association, and consequently the chairman of the nominating committee presented a slate of officers for election.

It was pointed out that the office of fourth vice-president was not being filled, inasmuch as there had not been sufficient time to obtain a candidate for this office. Under the provisions of the Constitution and By-laws, any office which is

vacant can be filled by the Council and it was left to the discretion of the Council to take necessary action.

Upon motion duly made, seconded, and carried, the slate of officers presented by the nominating committee were elected by the Association.

Election of Officers

At the annual meeting of the National Gastroenterological Association, held at the Hotel Statler in New York City, on Monday, 9 October 1950, the following new officers of the Association were elected for the year 1950-51 as indicated: President-elect, Dr. William W. Lermann, Pittsburgh, Pa.; first vice-president, Dr. Felix Cunha, San Francisco, Calif.; second vice-president, Dr. Harry M. Eberhard, Philadelphia, Pa.; third vice-president, Dr. Charles W. McClure, Boston, Mass.; secretary-general, Dr. Roy Upham, New York, N. Y.; secretary, Dr. Sigurd W. Johnsen, Passaic, N. J.; treasurer, Dr. Elihu Katz, New York, N. Y.

Under the provisions of the newly-adopted Constitution and By-laws, 20 Fellows were to be elected to the Council, and in order to provide for the provisions of the terms of office of five of the members expiring each year, the following were elected for a period of one year: Dr. Ludwig Frank, Charleston, W. Va.; Dr. Lynn A. Ferguson, Grand Rapids, Mich.; Dr. Henry A. Rafsky, New York, N. Y.; Dr. Lester Whitaker, Portsmouth, N. H.; Dr. Benjamin M. Bernstein, Brooklyn, N. Y. Those elected for a period of two years are Dr. Max Thorek, Chicago, Ill.; Dr. Frank J. Borrelli, Tuckahoe, N. Y.; Dr. Louis L. Perkel, Jersey City, N. J.; Dr. Fred H. Voss, Phoenicia, N. Y., and Dr. H. Necheles, Chicago, Ill. For three years the following were elected: Dr. Fernando Milanes, Havana, Cuba; Dr. John E. Cox, Memphis, Tenn.; Dr. S. Bernard Kaplan, Newark, N. J.; Dr. Jean LeSage, Montreal, Canada; Dr. James T. Nix, New Orleans, La. For the full four-year term the Association elected Dr. Donald C. Collins, Los Angeles, Calif.; Dr. Roland W. Ricketts, Merchantville, N. J.; Dr. William C. Jacobson, New York, N. Y.; Dr. Frank A. Cummings, Providence, R. I.; Dr. Samuel A. Berger, Cleveland, Ohio.

All of the above officers and members of the Council elected, as well as Dr. Horace W. Soper, past president, and Dr. Samuel Weiss, editor of The Review of Gastroenterology, comprise the new Council for the year 1950-51.

Meeting of the Executive Committee

A meeting of the newly-constituted Executive Committee of the National Council was held at the Hotel Statler in New York City, on Wednesday, 11 October 1950.

The Executive Committee sat as a committee of the whole to discuss the problem of the 1951 convention in Chicago, and to make recommendations for the program.

The matter of the appointment of new committees was tabled until the president, Dr. Tidmarsh, could have more time to study the matter.

The committee took under advisement several suggestions made by various members of the Council, and adjourned until its next meeting in New York City, on 5 November 1950.

Sixteenth Annual Convention

The Sixteenth Annual Convention of the National Gastroenterological Association will be held at the Hotel Drake in Chicago, Ill., on 17, 18, 19 September 1951.

The program committee consisting of Dr. C. J. Tidmarsh, Montreal, Canada, chairman; Dr. William W. Lermann, Pittsburgh, Pa., and Dr. Sigurd W. Johnsen, Passaic, N. J., have already started work on the new program and have received acceptances to invitations from several speakers.

Further details concerning the program will be published as they become available.

In Memoriam

We record with profound sorrow the passing of Dr. Christian W. Janson, Brooklyn, N. Y., Fellow of the National Gastroenterological Association.

We extend our deepest sympathies to the family.

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1. Weiss, S., et al.: Rev. Gastroenterology 16:501-509 (June) 1949.

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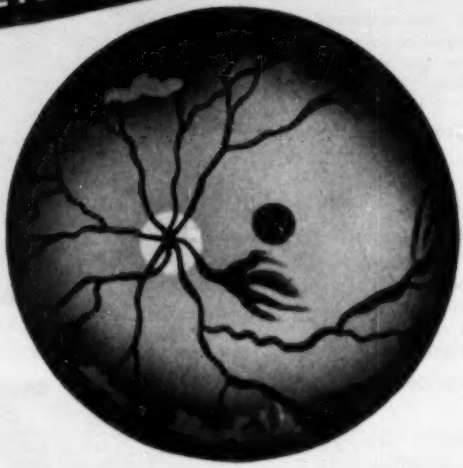

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Accumulating evidence[1,2] is more firmly establishing the ability of inositol to reduce abnormally high blood cholesterol levels. This lipotropic agent activity has been demonstrated not only in patients with liver disease, but also in the presence of diabetes mellitus.[3]

Since hypercholesterolemia is regarded as a forerunner of atherosclerosis which in turn leads to local or generalized arteriosclerosis, inositol constitutes a sound weapon for the prevention or active treatment of degenerative arterial disease. Although the lipotropic activity of inositol is evident in the absence of all other therapy, the use of a high protein, low fat diet and the administration of other B complex vitamins is also advisable.

Inositol-C.S.C., supplied in 0.5 Gm. tablets, is indicated whenever lipotropic action of this substance is required. Average dose, 1.0 Gm. three times daily.

(1.) Felch, W. C.: New York Med. 5:16 (Oct. 20) 1949. (2.) Leinwand, I., and Moore, D. H.: Am. Heart J. 18:467 (Sept.) 1940. (3.) Felch, W. C., and Datti, L. B.: Proc. Soc. Exper. Biol. & Med. 72:376 (Nov.) 1949.

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Creamalin relieves ulcer pain in minutes because it is truly *amorphous* aluminum hydroxide, the form emphasized by Sollmann[1] as being most soluble. Greater solubility makes Creamalin rapidly available for neutralization. Also, Creamalin is a *reactive* gel. Reactive gels exhibit greater acid-combining power.[2]

Creamalin heals the lesion in 7 to 10 days because it is *acid-soluble* aluminum hydroxide, the nonabsorbable antacid which provides sustained neutralization at pH 4 to pH 5. Healing is fast because Creamalin inhibits pepsin activity and is "mucosal adherent." Tablets and liquid.

1. Sollmann, T.: A Manual of Pharmacology. Philadelphia, W. B. Saunders Co., 7th ed., 1948, p. 938.
2. Batterman, R. C., and Ehrenfeld, I.: Gastroenterology, 9:141, Aug., 1947.

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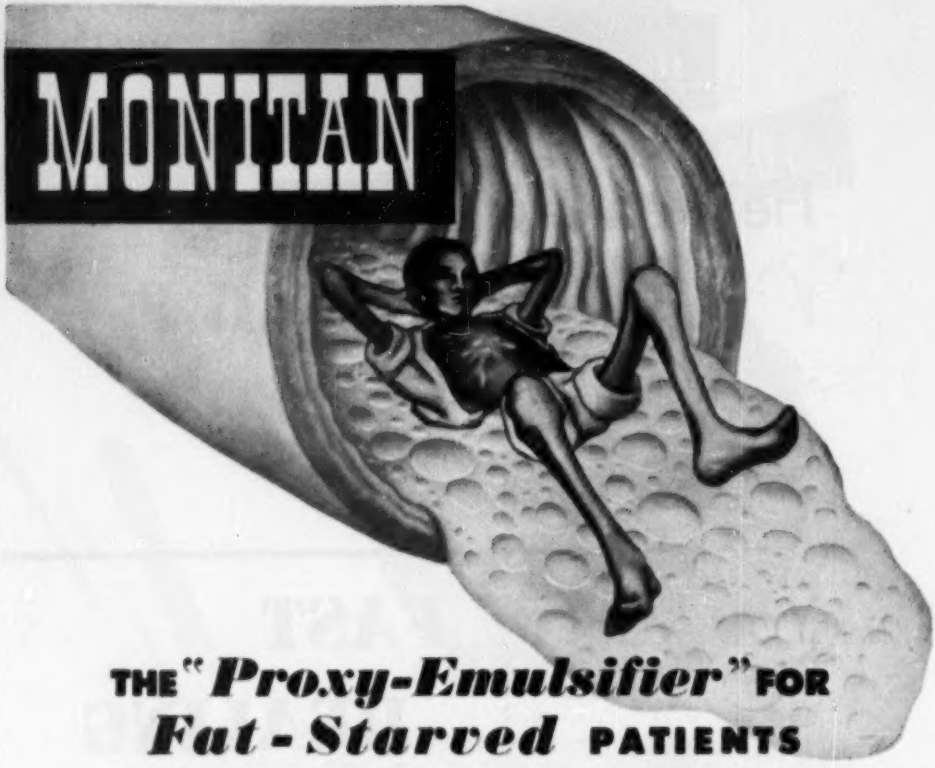

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Phenobarbital.....	¼ gr.
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Through central cerebral action and local parasympathetic blocking, Elixir Hybephen relieves the discomfort associated with smooth muscle hyperactivity in pylorospasm, cardiospasm, gastric hypermotility, spasticity of the colon and functional diarrhea. It achieves this objective through the combined influence of phenobarbital, tincture of belladonna, and tincture of hyoscyamus, all of which are incorporated in a palatable, pleasant vehicle.

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3. **Promotion of granulation tissue** (with tissue-stimulating chlorophyll). *Only Chloresium Powder gives this tissue-stimulating "bonus!"*

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*Offenkrantz, W. F., Rev. of Gastroenterology, 17:359-367 (May), 1950.

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[1]Seley, S. A.: Medical Management of Pyloric Obstruction Resulting from Peptic Ulcer, *Am. J. Dig. Dis., 13*:238, 1946.

*T. M. Reg. U. S. Pat. Off.

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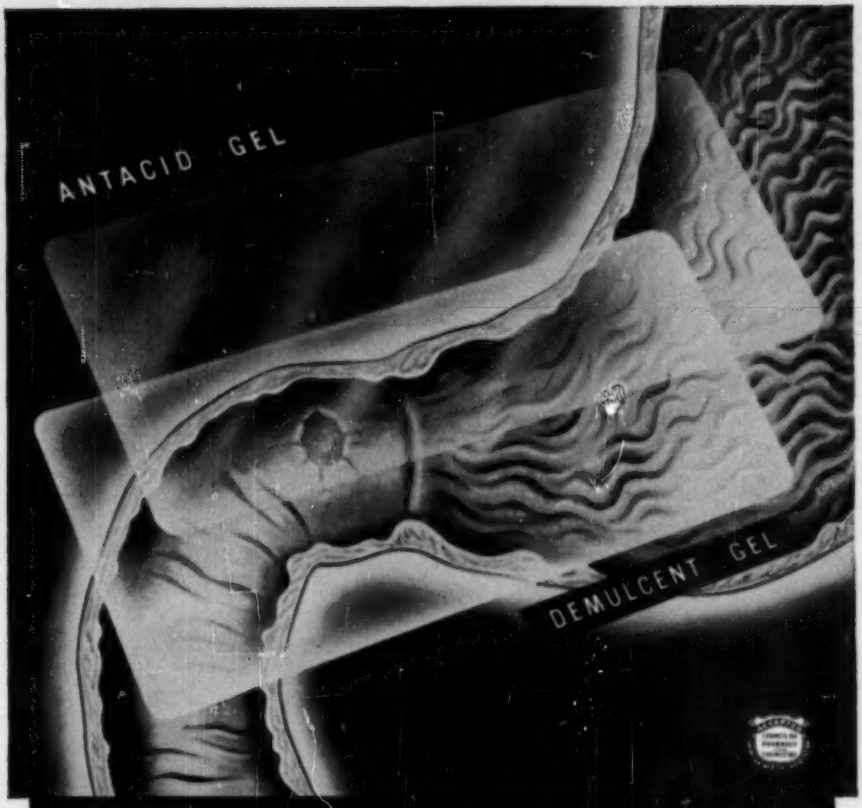

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